

chain nodes :

in nodes :

1	2	3	4	7	8	9	10	11	12	13	14	15	16	23	30	34
---	---	---	---	---	---	---	----	----	----	----	----	----	----	----	----	----

ring nodes :

24 25 26 27 28 29

chain bonds :

1-2 2-3 3-4 4-23 7-8 7-9 11-12 13-14 15-16 23-25 28-30

ring bonds :

24-25   24-29   25-26   26-27   27-28   28-29

exact/norm bonds :

1-2    3-4    4-23    28-30

exact bonds :

2-3 7-8 7-9 11-12 13-14 15-16 23-25 24-25 24-29 25-26 26-27 27-28 28-29

isolated ring systems :

containing 24 :

G1: [\*1], [\*2], [\*3], [\*4], [\*5], [\*6]

Match level :

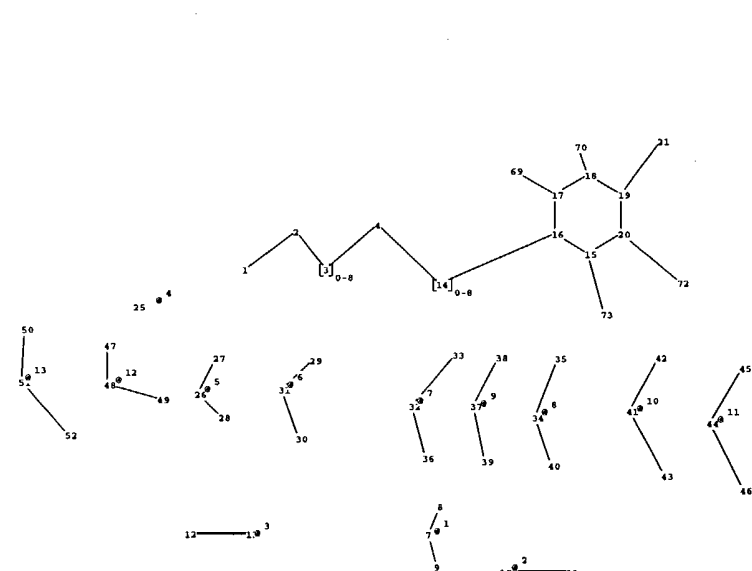
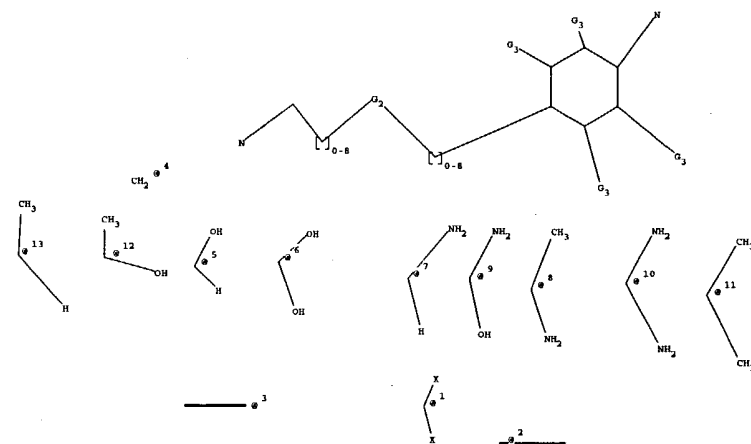
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1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS
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1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS
13:CLASS 14:CLASS 15:CLASS 16:CLASS 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom
```

```

15:CLASS      14:CLASS      13:CLASS      12:CLAS
28:Atom      29:Atom      30:CLASS      34:CLASS

```



chain nodes :  
 1 2 3 4 7 8 9 10 11 12 13 14 21 25 26 27 28 29 30 31 32 33 34 35 36  
 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 69 70 72 73

ring nodes :  
 15 16 17 18 19 20

chain bonds :  
 1-2 2-3 3-4 4-14 7-8 7-9 10-11 12-13 14-16 15-73 17-69 18-70 19-21 20-72  
 26-27 26-28 29-31 30-31 32-33 32-36 34-35 34-40 37-38 37-39 41-43 41-42 44-45  
 44-46 47-48 48-49 50-51 51-52

ring bonds :  
 15-16 15-20 16-17 17-18 18-19 19-20

exact/norm bonds :  
 1-2 3-4 4-14 15-73 17-69 18-70 19-21 20-72 26-27 29-31 30-31 32-33 34-40 37-38  
 37-39 41-43 41-42 48-49

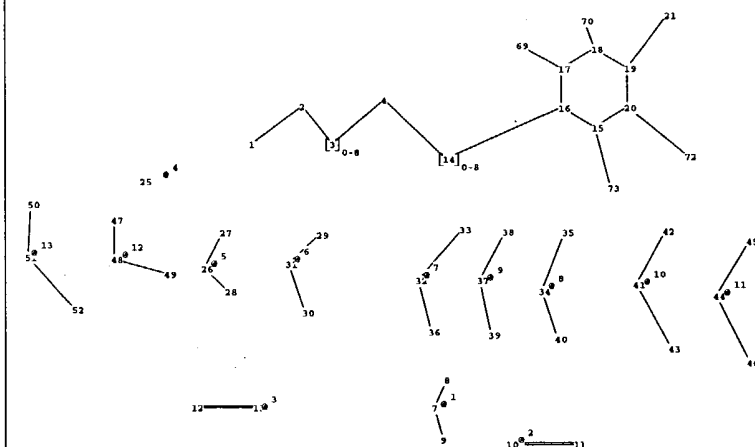
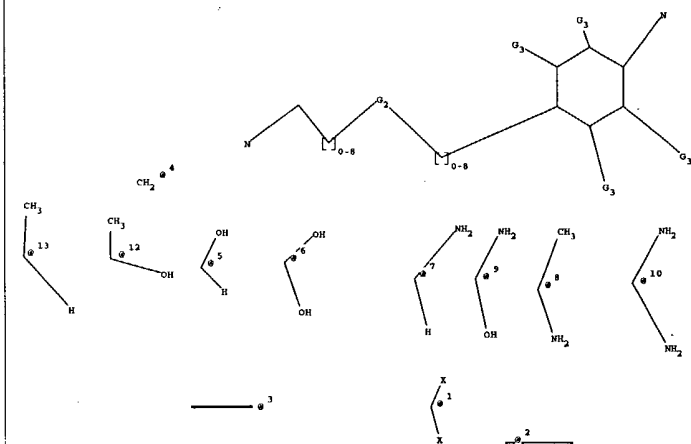
exact bonds :  
 2-3 7-8 7-9 10-11 12-13 14-16 15-16 15-20 16-17 17-18 18-19 19-20 26-28 32-36  
 34-35 44-45 44-46 47-48 50-51 51-52

isolated ring systems :  
 containing 15 :

G2:[\*1],[\*2],[\*3],[\*4],[\*5],[\*6],[\*7],[\*8],[\*9],[\*10],[\*11],[\*12],[\*13]

G3:H,CH3,OH,NH2

Match level :  
 1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS  
 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS  
 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS  
 34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS  
 43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS  
 52:CLASS 69:CLASS 70:CLASS 72:CLASS 73:CLASS



chain nodes :

1 2 3 4 7 8 9 10 11 12 13 14 21 25 26 27 28 29 30 31 32 33 34 35 36  
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 69 70 72 73

ring nodes :

15 16 17 18 19 20

chain bonds :

1-2 2-3 3-4 4-14 7-8 7-9 10-11 12-13 14-16 15-73 17-69 18-70 19-21 20-72  
26-27 26-28 29-31 30-31 32-33 32-36 34-35 34-40 37-38 37-39 41-43 41-42 44-45  
44-46 47-48 48-49 50-51 51-52

ring bonds :

15-16 15-20 16-17 17-18 18-19 19-20

exact/norm bonds :

1-2 3-4 4-14 15-73 17-69 18-70 19-21 20-72 26-27 29-31 30-31 32-33 34-40 37-38  
37-39 41-43 41-42 48-49

exact bonds :

2-3 7-8 7-9 10-11 12-13 14-16 15-16 15-20 16-17 17-18 18-19 19-20 26-28 32-36  
34-35 44-45 44-46 47-48 50-51 51-52

isolated ring systems :

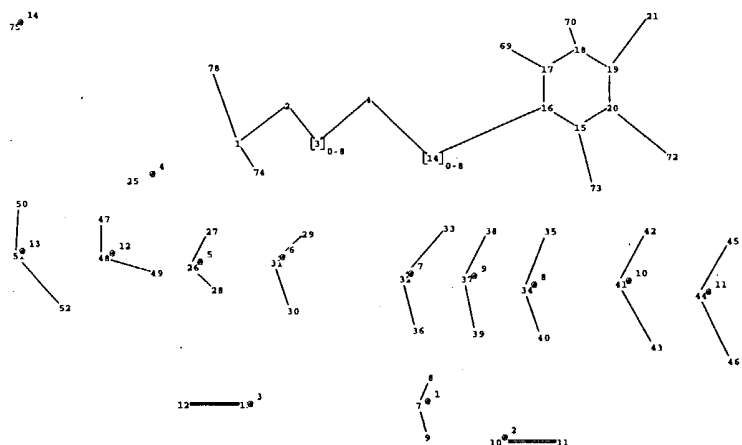
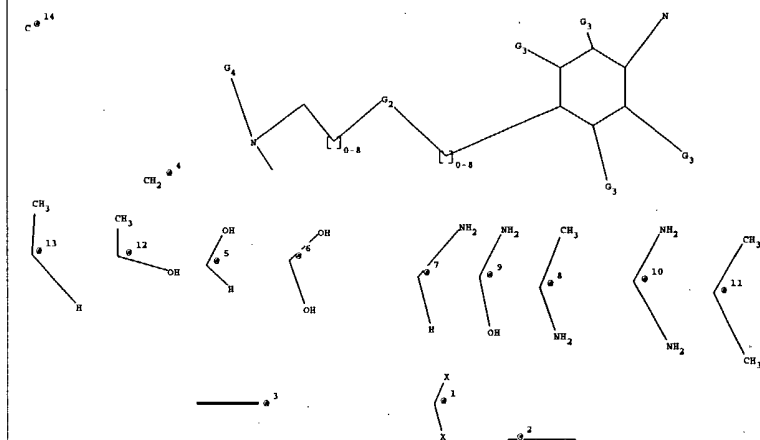
containing 15 :

G2:[\*1],[\*2],[\*3],[\*4],[\*5],[\*6],[\*7],[\*8],[\*9],[\*10],[\*11],[\*12],[\*13]

G3:H,CH3,OH,NH2

Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS  
13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS  
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS  
34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS  
43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS  
52:CLASS 69:CLASS 70:CLASS 72:CLASS 73:CLASS



chain nodes :

1 2 3 4 7 8 9 10 11 12 13 14 21 25 26 27 28 29 30 31 32 33 34 35 36  
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 69 70 72 73 74 75 78

ring nodes :

15 16 17 18 19 20

chain bonds :

1-2 1-74 1-78 2-3 3-4 4-14 7-8 7-9 10-11 12-13 14-16 15-73 17-69 18-70 19-21  
20-72 26-27 26-28 29-31 30-31 32-33 32-36 34-35 34-40 37-38 37-39 41-43 41-42  
44-45 44-46 47-48 48-49 50-51 51-52

ring bonds :

15-16 15-20 16-17 17-18 18-19 19-20

exact/norm bonds :

1-2 1-74 1-78 3-4 4-14 15-73 17-69 18-70 19-21 20-72 26-27 29-31 30-31 32-33  
34-40 37-38 37-39 41-43 41-42 48-49

exact bonds :

2-3 7-8 7-9 10-11 12-13 14-16 15-16 15-20 16-17 17-18 18-19 19-20 26-28 32-36  
34-35 44-45 44-46 47-48 50-51 51-52

isolated ring systems :

containing 15 :

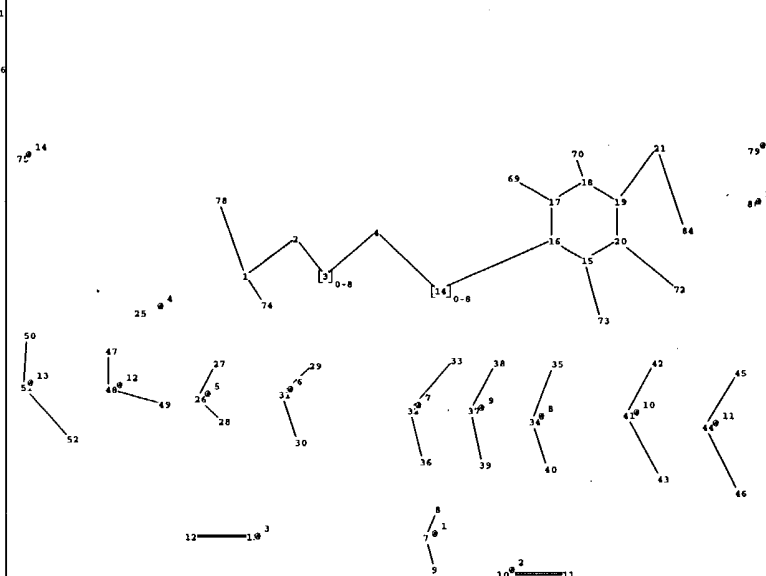
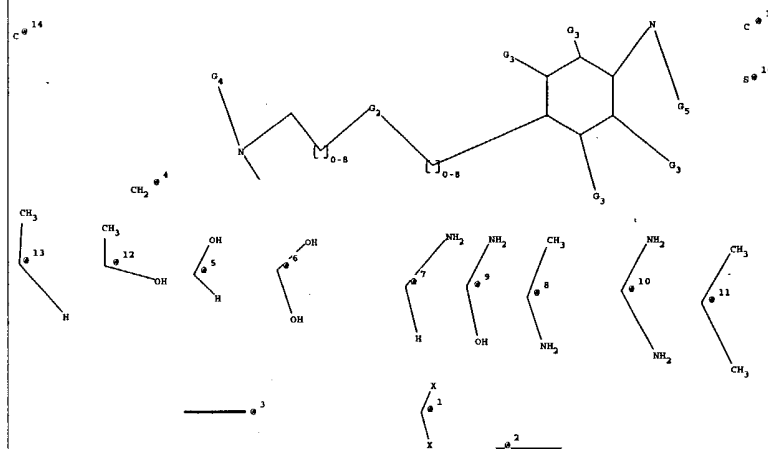
G2:[\*1],[\*2],[\*3],[\*4],[\*5],[\*6],[\*7],[\*8],[\*9],[\*10],[\*11],[\*12],[\*13]

G3:H,CH3,OH,NH2

G4:H,[\*14]

Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS  
13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS  
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS  
34:CLASS 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 42:CLASS  
43:CLASS 44:CLASS 45:CLASS 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS 51:CLASS  
52:CLASS 69:CLASS 70:CLASS 72:CLASS 73:CLASS 74:CLASS 75:CLASS 78:CLASS



## chain nodes :

1 2 3 4 7 8 9 10 11 12 13 14 21 25 26 27 28 29 30 31 32 33 34 35 36  
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 69 70 72 73 74 75 78  
79 80 84

## ring nodes :

15 16 17 18 19 20

## chain bonds :

1-2 1-74 1-78 2-3 3-4 4-14 7-8 7-9 10-11 12-13 14-16 15-73 17-69 18-70 19-21  
20-72 21-84 26-27 26-28 29-31 30-31 32-33 32-36 34-35 34-40 37-38 37-39 41-43  
41-42 44-45 44-46 47-48 48-49 50-51 51-52

## ring bonds :

15-16 15-20 16-17 17-18 18-19 19-20

## exact/norm bonds :

1-2 1-74 1-78 3-4 4-14 15-73 17-69 18-70 19-21 20-72 21-84 26-27 29-31 30-31  
32-33 34-40 37-38 37-39 41-43 41-42 48-49

## exact bonds :

2-3 7-8 7-9 10-11 12-13 14-16 15-16 15-20 16-17 17-18 18-19 19-20 26-28 32-36  
34-35 44-45 44-46 47-48 50-51 51-52

## isolated ring systems :

containing 15 :

G2:[\*1],[\*2],[\*3],[\*4],[\*5],[\*6],[\*7],[\*8],[\*9],[\*10],[\*11],[\*12],[\*13]

G3:H,CH3,OH,NH2

G4:H,[\*14]

G5:[\*15],[\*16]

## Match level :

1:CLASS 2:CLASS 3:CLASS 4:CLASS 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS  
13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:CLASS  
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS  
34:CLASS

43:CLASS	35:CLASS	36:CLASS	37:CLASS	38:CLASS	39:CLASS	40:CLASS	41:CLASS	42:CLASS
44:CLASS	44:CLASS	45:CLASS	46:CLASS	47:CLASS	48:CLASS	49:CLASS	50:CLASS	51:CLASS
52:CLASS	69:CLASS	70:CLASS	72:CLASS	73:CLASS	74:CLASS	75:CLASS	78:CLASS	79:CLASS
80:CLASS	84:CLASS							

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 and searchable  
 NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in  
 CA/CAPLUS  
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 changes  
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 NEWS 11 MAR 29 No connect hour charges in WPIFV until May 1, 2004  
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	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

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DICTIONARY FILE UPDATES: 23 APR 2004 HIGHEST RN 676578-75-9

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=>

L1 STRUCTURE UPLOADED

=> s l1

SAMPLE SEARCH INITIATED 03:47:32 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 20904 TO ITERATE

4.8% PROCESSED 1000 ITERATIONS 1 ANSWERS  
 INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*INCOMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 409433 TO 426727  
 PROJECTED ANSWERS: 144 TO 692

L2 1 SEA SSS SAM L1

=>

L3 STRUCTURE UPLOADED

=> s l3

SAMPLE SEARCH INITIATED 03:50:11 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 19474 TO ITERATE

5.1% PROCESSED 1000 ITERATIONS 1 ANSWERS  
 INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)  
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 381132 TO 397828  
 PROJECTED ANSWERS: 125 TO 653

L4 1 SEA SSS SAM L3

=> s l3 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS  
 DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y  
 FULL SEARCH INITIATED 03:50:18 FILE 'REGISTRY'  
 FULL SCREEN SEARCH COMPLETED - 390406 TO ITERATE

100.0% PROCESSED 390406 ITERATIONS 281 ANSWERS  
 SEARCH TIME: 00.00.05

L5 281 SEA SSS FUL L3

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
157.94	158.15

FULL ESTIMATED COST



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 FILE LAST UPDATED: 25 Apr 2004 (20040425/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 15

L6 58 L5

=> s 16 and ackermann, j?/au

172 ACKERMANN, J?/AU

L7 2 L6 AND ACKERMANN, J?/AU

=> d 17, ibib abs fhitstr, 1-2

L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

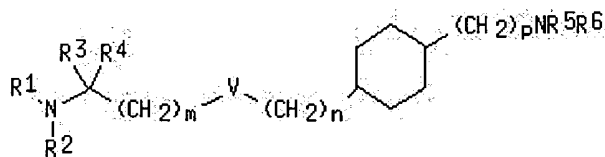
Full Text Citing References

ACCESSION NUMBER: 2003:511301 HCAPLUS  
 DOCUMENT NUMBER: 139:85041  
 TITLE: Heteroaryl-substituted aminocyclohexane derivatives as inhibitors of 2,3-oxidosqualene lanosterol cyclase  
 INVENTOR(S): Ackermann, Jean; Aebi, Johannes; Dehmlow, Henrietta; Maerki, Hans-Peter; Morand, Olivier  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 83 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

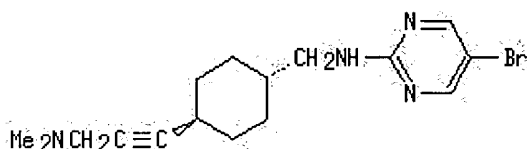
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003053933	A1	20030703	WO 2002-EP14037	20021211
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PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG

US 2003186984 A1 20031002 US 2002-310559 20021205  
PRIORITY APPLN. INFO.: EP 2001-130284 A 20011220  
OTHER SOURCE(S): MARPAT 139:85041  
GI



I



II

AB Title compds. I [R1 = H, alkyl, hydroxyalkyl, alkenyl; R2 = (un)substituted alkyl, cycloalkyl, cycloalkylalkyl, alkenyl; NR1R2 = heterocyclic; R3, R4 = H, alkyl; R3R4 = (CH2)5; R5 = H, alkyl, alkenyl; R6 = (un)substituted pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl; V = bond, O, S, CH:CHCH2O, CH:CH, C≡C; m, n = 0-7; p = 0-2] and their N-oxides were prepd. for use as 2,3-oxidosqualene lanosterol cyclase inhibitors in treating diseases such as hypercholesterolemia, hyperlipemia, arteriosclerosis, vascular diseases, mycoses, parasitic infections, gallstones, tumors and/or hyperproliferative disorders, and treatment and/or prophylaxis of impaired glucose tolerance and diabetes. Thus, trans-3-{4-[(5-bromo-2-pyrimidinyl)methylamino]cyclohexyl}prop-2-yn-1-ol, prepd. from trans-4-tert.-butoxycarbonylaminocyclohexanecarboxylic acid and 2,5-dibromopyrimidine via trans-3-(4-methylaminocyclohexyl)prop-2-yn-1-ol, was converted to its mesylate and treated with Me2NH to give the title compd. II.

IT 553676-54-3P

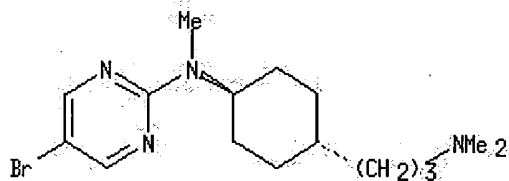
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heteroaryl-substituted aminocyclohexane derivs. as inhibitors of 2,3-oxidosqualene lanosterol cyclase)

RN 553676-54-3 HCAPLUS

CN 2-Pyrimidinamine, 5-bromo-N-[trans-4-[3-(dimethylamino)propyl]cyclohexyl]-N-methyl- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

5

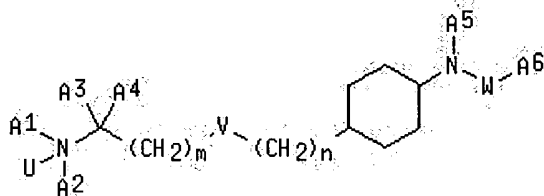
THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

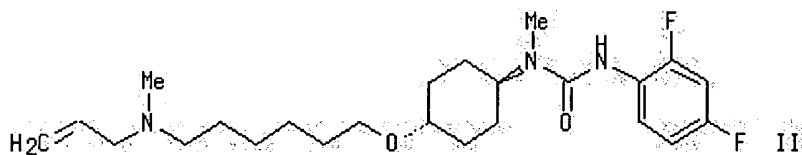
Full Text Citing References

ACCESSION NUMBER: 2002:142662 HCAPLUS  
 DOCUMENT NUMBER: 136:199955  
 TITLE: Preparation of aminocyclohexanes as OSC inhibitors for treatment of hypercholesterolemia, hyperlipemia, arteriosclerosis, and vascular diseases  
 INVENTOR(S): Ackermann, Jean; Aebl, Johannes; Blum, Denise; Chucholowski, Alexander; Dehmlow, Henrietta; Maerki, Hans-Peter; Morand, Olivier; Trussardi, Rene; Von der Mark, Elisabeth; Wallbaum, Sabine; Weller, Thomas  
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.  
 SOURCE: PCT Int. Appl., 221 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014267	A1	20020221	WO 2001-EP9174	20010808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001093744	A5	20020225	AU 2001-93744	20010808
EP 1311475	A1	20030521	EP 2001-974142	20010808
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BR 2001013408	A	20030617	BR 2001-13408	20010808
JP 2004506037	T2	20040226	JP 2002-519412	20010808
RU 2225393	C1	20040310	RU 2003-105818	20010808
US 2002045777	A1	20020418	US 2001-925188	20010809
NO 2003000657	A	20030213	NO 2003-657	20030210
PRIORITY APPLN. INFO.:			EP 2000-117611	A 20000816
			EP 2001-113646	A 20010619
			WO 2001-EP9174	W 20010808
OTHER SOURCE(S):			MARPAT 136:199955	
GI				



I



II

AB Title compds. I [wherein U = O or a lone pair; V = O, S, CH<sub>2</sub>, CH:CH, or C≡C; W = CO, CO<sub>2</sub>, CONR<sub>1</sub>, CSO, CSNR<sub>1</sub>, SO<sub>2</sub>, or SO<sub>2</sub>NR<sub>1</sub>; m and n = independently 0-7 and m + n = 0-7, with provisos; A<sub>1</sub> = H, (hydroxy)alkyl, or alkenyl; A<sub>2</sub> = (un)substituted alkyl, cycloalkyl(alkyl), or alkenyl; A<sub>3</sub> and A<sub>4</sub> = independently H or alkyl; or A<sub>1</sub> and A<sub>2</sub> or A<sub>1</sub> and A<sub>3</sub> or A<sub>3</sub> and A<sub>4</sub> may form a ring; A<sub>5</sub> = H, (aryl)alkyl, or alkenyl; A<sub>6</sub> = (cyclo)alkyl, aryl(alkyl), heteroaryl(alkyl), or alkoxycarbonylalkyl; R<sub>1</sub> = H or alkyl; and pharmaceutically acceptable salts and/or esters thereof] were prepd. Thus, trans-(4-hydroxycyclohexyl)methylcarbamate acid tert-Bu ester (prepn. given) was etherified with 1,6-dibromohexane. Addn. of N-allylmethylamine, followed by deprotection using TFA, afforded trans-[4-[4-(N-allylmethylamino)hexyloxy]cyclohexyl]methylamine. Coupling of the amine with 2,4-difluorophenylisocyanate in dioxane gave II. I are useful for the treatment and/or prophylaxis of diseases which are assocd. with 2,3-oxidosqualene-lanosterol cyclase (OSC), such as hypercholesterolemia, hyperlipemia, arteriosclerosis, vascular diseases, mycoses, gallstones, tumors and/or hyperproliferative disorders, and treatment and/or prophylaxis of impaired glucose tolerance and diabetes (no data).

## IT 400897-20-3P

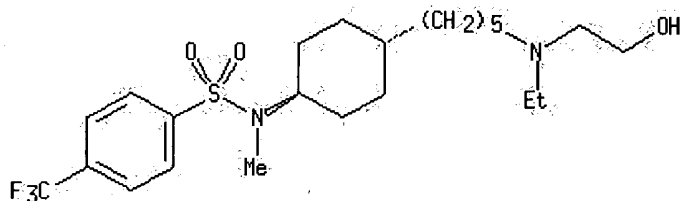
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(OSC inhibitor; prepn. of aminocyclohexanes as OSC inhibitors for treatment of hypercholesterolemia, hyperlipemia, arteriosclerosis, and vascular diseases)

RN 400897-20-3 HCAPLUS

CN Benzenesulfonamide, N-[trans-4-[5-[ethyl(2-hydroxyethyl)amino]pentyl]cyclohexyl]-N-methyl-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 03:46:20 ON 26 APR 2004)

FILE 'REGISTRY' ENTERED AT 03:46:26 ON 26 APR 2004

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L1      STRUCTURE UPLOADED
L2      1 S L1
L3      STRUCTURE UPLOADED
L4      1 S L3
L5      281 S L3 FULL
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FILE 'HCAPLUS' ENTERED AT 03:50:26 ON 26 APR 2004

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L7      2 S L6 AND ACKERMANN, J?/AU
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=> s 16 not 17
L8      56 L6 NOT L7
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L9      0 L8 AND AEEL, J?/AU
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L14     0 L8 AND MORAND, O?/AU
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L8      ANSWER 1 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
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Full Text	Citing References
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ACCESSION NUMBER: 2004:282867 HCAPLUS  
 TITLE: Preparation of peptide antiangiogenic drugs  
 INVENTOR(S): Henkin, Jack; Haviv, Fortuna; Bradley, Michael F.;  
 Calvin, Douglas M.; Schneider, Andrew J.  
 PATENT ASSIGNEE(S): Abbott Laboratories, USA  
 SOURCE: U.S., 84 pp., Cont.-in-part of U.S. Ser. No. 316,888.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6716963	B1	20040406	US 1999-447226	19991122
PRIORITY APPLN. INFO.:			US 1998-86536P	P 19980522
			US 1999-126546P	P 19990326
			US 1999-316888	A2 19990521

AB Peptides A0-A1-A2-A3-A4-A5-A6-A7-A8-A9-A10 (A0 is an acyl group; A10 is OH, an amino group, or an amino acid amide; A1-9 are amino acyl residues) or their pharmaceutically acceptable salts, esters, solvates, or prodrugs were prepd. for the treatment of angiogenesis. Thus, N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-Pro-NHET was prepd. by the solid-phase method and assayed for in vitro angiogenic activity (87.3 and 76.9% inhibition at 20 nM and 10 nM. resp.).

IT 251900-41-1P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

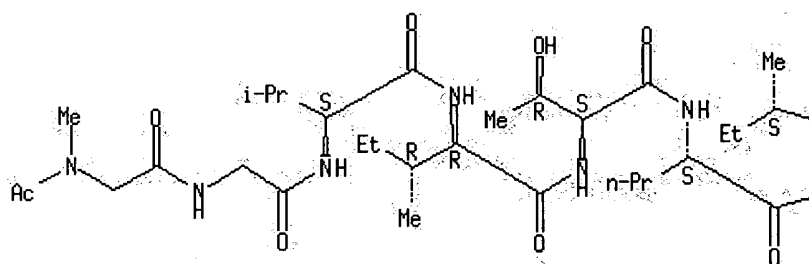
(prepn. of peptide antiangiogenic drugs)

RN 251900-41-1 HCAPLUS

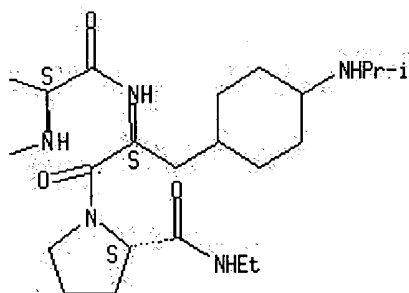
CN L-Prolinamide, N-acetyl-N-methylglycylglycyl-L-valyl-D-isoleucyl-L-threonyl-L-norvalyl-L-isoleucyl-3-[4-[(1-methylethyl)amino]cyclohexyl]-L-alanyl-N-ethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

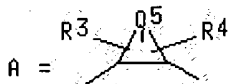
L8 ANSWER 2 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2003:508525 HCAPLUS  
 DOCUMENT NUMBER: 139:85363  
 TITLE: Preparation of diamine derivatives as factor Xa inhibitors and anticoagulants, and their use for treatment of diseases  
 INVENTOR(S): Ota, Toshiharu; Komoritani, Satoshi; Yoshino, Toshiharu; Uoto, Koichi; Nakamoto, Yumi; Naito, Hiroyuki; Mochizuki, Akiyoshi; Nagata, Tsutomu; Kanno, Hideyuki; Haginoya, Noriyasu; Yoshikawa, Kenji; Nagamochi, Masatoshi; Kobayashi, Shozo  
 PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 284 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003183286	A2	20030703	JP 2001-398959	20011228
PRIORITY APPLN. INFO.:			JP 2001-311909	A 20011009
OTHER SOURCE(S):		MARPAT 139:85363		

GI



AB The derivs. are Q1Q2T0NR1Q3NR2R1Q4 [Q1 = (substituted) 5- to 6-membered cyclic hydrocarbonyl, (substituted) 5- to 7-membered heterocyclyl, etc.; Q2 = single bond, (substituted) 5- to 6-membered cyclic hydrocarbonylene, etc.; Q3 = A; Q4 = (substituted) aryl, (substituted) arylalkenyl, etc.; Q5 = C1-8 alkylene, C2-8 alkenylene, etc.; T0 = (thio)carbonyl; T1 = carbonyl, sulfonyl, etc.; R1, R2 = H, OH, alkyl, alkoxy; R3, R4 = H, OH, alkyl, etc.], their salts, solvates, or N-oxides. Thus, (±)-trans-N-[(5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridin-2-yl)carbonyl]-1,2-cyclopentanediimine HCl salt was amidated with 5-chloroindole-2-carboxylic acid to give I which inhibited human factor Xa with IC50 86 nM in vitro.

IT 552849-54-4P

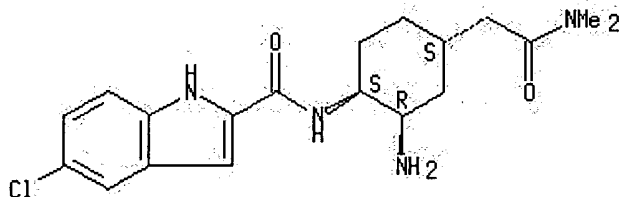
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of diamine derivs. as factor Xa inhibitors for anticoagulants)

RN 552849-54-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1R,2S,4R)-2-amino-4-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]-5-chloro-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 3 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2003:282325 HCAPLUS  
DOCUMENT NUMBER: 138:321285  
TITLE: Preparation of quinazoline-2,4-diamines as MCH receptor antagonists  
INVENTOR(S): Sekiguchi, Yoshinori; Kanuma, Kosuke; Omodera, Katsunori; Tran, Thuy-anh; Kramer, Bryan Aubrey; Beeley, Nigel Robert Arnold  
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 1171 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028641	A2	20030410	WO 2002-US31059	20020930
WO 2003028641	A3	20030828		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-326463P P 20011001  
US 2001-326758P P 20011002

OTHER SOURCE(S): MARPAT 138:321285  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*



AB The title compds. QLYR1[Q = I, C(:NH)NH<sub>2</sub>; R<sub>1</sub> = (un)substituted alkyl, alkenyl, cycloalkyl, etc.; L = II-IV (wherein R<sub>4</sub> = H, alkyl; R<sub>5</sub> = H, alkyl, alkyl substituted by a substituted carbocyclic aryl), etc.; Y = SO<sub>2</sub>, CO, (CH<sub>2</sub>)<sub>m</sub>; m = 0-1] which act as MCH receptor antagonists, and are useful for prophylaxis or treatment of obesity, obesity related disorders, anxiety, or depression, were prepd. Thus, hydrogenation of benzyl cis-[4-(4-dimethylaminoquinazolin-2-ylamino)cyclohexylmethyl]carbamate followed by reacting the resulting intermediate with 4-bromo-2-trifluoromethoxybenzaldehyde in the presence of NaBH(OAc)<sub>3</sub> and AcOH in CH<sub>2</sub>Cl<sub>2</sub>, and treatment of the product with 4N HCl in EtOAc afforded 34% cis-V.2HCl which showed IC<sub>50</sub> of 6 nM against MCH receptor.

IT 509142-96-5P

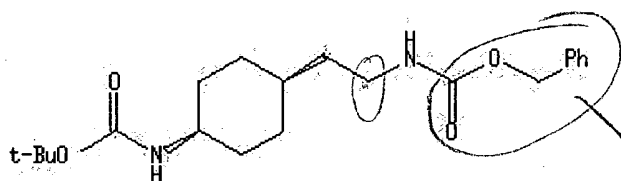
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of quinazoline-2,4-diamines as MCH receptor antagonists)

RN 509142-96-5 HCAPLUS

CN Carbamic acid, [2-[cis-4-[[[(1,1-dimethylethoxy)carbonyl]amino]cyclohexyl]ethyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 4 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2003:154422 HCAPLUS  
 DOCUMENT NUMBER: 138:205076  
 TITLE: Preparation of diamines as factor Xa inhibitors  
 INVENTOR(S): Ohta, Toshiharu; Komoriya, Satoshi; Yoshino, Toshiharu; Uoto, Kouichi; Nakamoto, Yumi; Naito, Hiroyuki; Mochizuki, Akiyoshi; Nagata, Tsutomu; Kanno, Hideyuki; Haginoya, Noriyasu; Yoshikawa, Kenji; Nagamochi, Masatoshi; Kobayashi, Syozo; Ono, Makoto  
 PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 847 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016302	A1	20030227	WO 2002-JP8119	20020808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,				

NE, SN, TD, TG

WO 2003000657	A1	20030103	WO 2002-JP2683	20020320
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WO 2003000680	A1	20030103	WO 2002-JP6141	20020620
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PRIORITY APPLN. INFO.:  
 JP 2001-243046 A 20010809  
 JP 2001-311808 A 20011009  
 JP 2001-398708 A 20011228  
 WO 2002-JP2683 A 20020320  
 WO 2002-JP6141 A 20020620  
 JP 2001-187105 A 20010620

OTHER SOURCE(S): MARPAT 138:205076  
 GI



AB The title compds. Q1-Q2-T0-N(R1)-Q3-N(R2)-T1-Q4 [R1 and R2 represent each hydrogen, etc.; Q1 represents optionally substituted, satd. or unsatd. 5- or 6-membered hydrocarbyl, etc.; Q2 represents a single bond, etc.; Q3 represents I wherein Q5 represents C1-8 alkylene, etc.; R3, R4 represent each hydrogen, alkyl, etc.; Q4 represents (un)substituted aryl, etc.; and T0 and T1 represent each carbonyl, etc.] are prepd. I are useful as antithrombotics, etc. Several compds. of this invention showed IC50 values of 1.2 nM to 3.5 nM against factor Xa.

IT 500572-01-0P

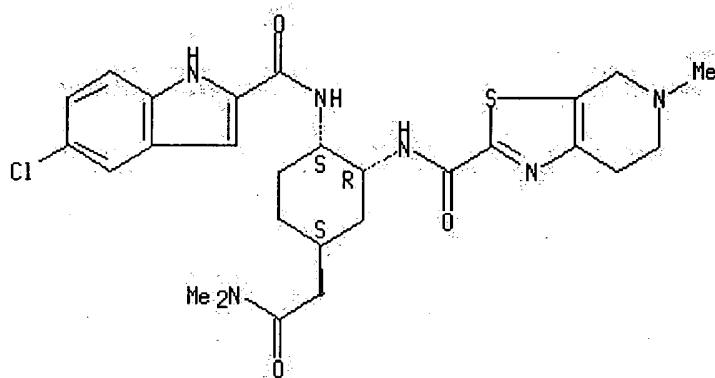
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of diamines as factor Xa inhibitors)

RN 500572-01-0 HCAPLUS

CN Thiazolo[5,4-c]pyridine-2-carboxamide, N-[(1R,2S,5S)-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-5-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]-4,5,6,7-tetrahydro-5-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



# HCl

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2003:5949 HCAPLUS  
 DOCUMENT NUMBER: 138:89801  
 TITLE: Preparation of heterocyclic moiety-containing diamine derivatives as FXa inhibitors  
 INVENTOR(S): Ohta, Toshiharu; Komoriya, Satoshi; Yoshino, Toshiharu; Uoto, Kouichi; Nakamoto, Yumi; Naito, Hiroyuki; Mochizuki, Akiyoshi; Nagata, Tsutomu; Kanno, Hideyuki; Haginoya, Noriyasu; Yoshikawa, Kenji; Nagamochi, Masatoshi; Kobayashi, Syozo; Ono, Makoto  
 PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 811 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000680	A1	20030103	WO 2002-JP6141	20020620
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WO 2003000657	A1	20030103	WO 2002-JP2683	20020320
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EP 1405852 A1 20040407 EP 2002-743653 20020620

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

WO 2003016302 A1 20030227 WO 2002-JP8119 20020808

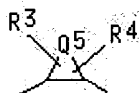
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

JP 2001-187105 A 20010620  
 JP 2001-243046 A 20010809  
 JP 2001-311808 A 20011009  
 JP 2001-398708 A 20011228  
 WO 2002-JP2683 W 20020320  
 WO 2002-JP6141 W 20020620

OTHER SOURCE(S): MARPAT 138:89801  
 GI



AB The title compds. Q1-Q2-T0-N(R1)-Q3-N(R2)-T1-Q4 [R1 and R2 represent each hydrogen, etc.; Q1 represents optionally substituted, satd. or unsatd. 5- or 6-membered hydrocarbonyl, etc.; Q2 represents a single bond, etc.; Q3 represents I (wherein Q5 represents C1-8 alkylene, etc.; R3, R4 represent each hydrogen, etc.); Q4 represents (un)substituted aryl, etc.; and T0 and T1 represent each carbonyl, etc.] are prepd. These compds. are useful as preventives and/or remedies for brain infarction, cerebral embolism, myocardial infarction, angina, thrombosis, etc. Compds. of this invention in vitro showed IC50 values of 1.4 nM to 92 nM against human FXa.

## IT 480448-97-3P

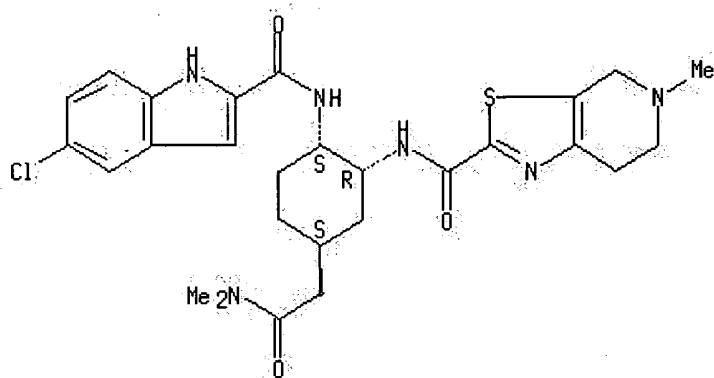
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of heterocyclic moiety-contg. diamine derivs. as FXa inhibitors)

RN 480448-97-3 HCAPLUS

CN Thiazolo[5,4-c]pyridine-2-carboxamide, N-[(1R,2S,5S)-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-5-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]-4,5,6,7-tetrahydro-5-methyl-, monohydrochloride, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



# HCl

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER: 2003:5928 HCAPLUS  
DOCUMENT NUMBER: 138:73271  
TITLE: Preparation of N,N'-bis(heterocyclic acyl)cycloalkanediamine and heterocyclediamine derivatives as inhibitors of activated blood coagulation factor X (factor Xa)  
INVENTOR(S): Ohta, Toshiharu; Komoriya, Satoshi; Yoshino, Toshiharu; Uoto, Kouichi; Nakamoto, Yumi; Naito, Hiroyuki; Mochizuki, Akiyoshi; Nagata, Tsutomu; Kanno, Hideyuki; Haginoya, Noriyasu; Yoshikawa, Kenji; Nagamochi, Masatoshi; Kobayashi, Syozo; Ono, Makoto  
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan  
SOURCE: PCT Int. Appl., 788 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003000657	A1	20030103	WO 2002-JP2683	20020320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2003000680	A1	20030103	WO 2002-JP6141	20020620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1405852 A1 20040407 EP 2002-743653 20020620

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

WO 2003016302 A1 20030227 WO 2002-JP8119 20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

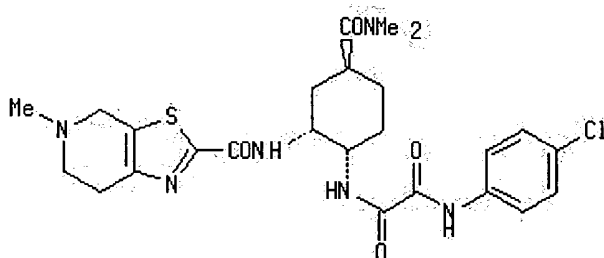
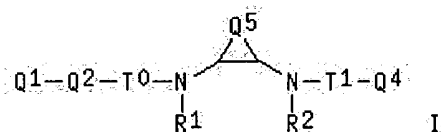
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

JP 2001-187105 A 20010620  
 JP 2001-243046 A 20010809  
 JP 2001-311808 A 20011009  
 JP 2001-398708 A 20011228  
 WO 2002-JP2683 W 20020320  
 WO 2002-JP6141 W 20020620

OTHER SOURCE(S):  
 GI

MARPAT 138:73271



AB Diamine compds. represented by the following general formula [I; wherein R1, R2 = H, HO, alkoxy; Q1 = each (un)substituted and (un)satd. 5 or 6-membered cyclic hydrocarbonyl, 5 to 7-membered heterocyclyl, or bicyclic or tricyclic fused hydrocarbonyl or heterocyclyl; Q2 = a single bond, (un)substituted and (un)satd. bivalent cyclic hydrocarbon, 5 to 7-membered heterocycle, or bicyclic or tricyclic fused hydrocarbon or heterocyclic group; Q5 = C1-8 alkylene, C2-8 alkenylene, (CH2)mCH2-A-CH2(CH2)n (wherein m, n = an integer of 0-3); A = O, N, S, SO, SO2, NH, ONH, NHNH, SNH, SONH, SO2NH; R3 and R4 are groups substituted on C, N, or S in the ring contg. Q5 and are selected from H, HO, alkyl, alkenyl, alkynyl, halo, haloalkyl, cyano, cyanoalkyl, NH2, aminoalkyl, N-alkylaminoalkyl, N,N-dialkylaminoalkyl, acyl, acylalkyl, (un)substituted acylaminoalkyl,

etc.; Q4 = each (un)substituted aryl, arylalkenyl, arylalkynyl, heteroaryl, or heteroarylalkenyl, each (un)satd. and (un)satd. bicyclic or tricyclic fused hydrocarbonyl or heterocyclonyl; T0 = CO, thiocarbonyl; T1 = CO, SO<sub>2</sub>, CO-CO, N-(un)substituted CO-NR, C(:S)-CO-NR, CO-C(S)-NR, C(S)-C(:S)-NR (wherein R = H, HO, alkyl, alkoxy), etc.], salts thereof, solvates of the same, or N-oxides of the same are prepd. The diamine compds. include N,N'-bis(heterocyclic acyl)-1,2-cyclopropanediamine, -1,2-cyclobutanediamine, 1,2-cyclopentanediamine, -1,2-cyclohexanediamine, 1,2-cycloheptanediamine, -1,2-cyclooctanediamine, -tetrahydro-3,4-furandiamine, -3,4-pyrrolidinediamine, -3,4-piperidinediamine, -tetrahydro-6-oxo-3,4-pyrandiamine, and -tetrahydro-3,4-thiopyrandiamine-1,1-dioxide derivs. These compds. are blood coagulation inhibitors and useful as preventives and/or remedies for thrombus or embolism including brain infarction, cerebral embolism, cardiac infarction, angina, pulmonary infarction, pulmonary embolism, Buerger's disease, deep venous thrombosis, disseminated intravascular coagulation syndrome, thrombosis following artificial flap/joint replacement, thrombosis and re-obstruction following blood flow reconstruction, systemic inflammatory reaction syndrome (SIRS), multiple organ dysfunction syndrome (MODS), thrombosis during external circulation or blood coagulation during blood collection. Thus, 288 mg 2-(4-chloroanilino)-2-oxoacetic acid Et ester was dissolved in 8.0 mL THF, treated with 46 mg LiOH and 1.0 mL H<sub>2</sub>O, stirred at room temp. for 2 h, concd. in dryness under reduced pressure to give 292 mg crude 2-(4-chloroanilino)-2-oxoacetic acid lithium salt (II). II and N-[(1R,2S,5S)-2-amino-5-[(dimethylamino)carbonyl]cyclohexyl]-5-methyl-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridine-2-carboxamide (prepn. given) were dissolved in 15 mL DMF and stirred with 164 mg 1-hydroxybenzotriazole hydrate and 251 mg 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride at room temp. for 64.5 h to give a cyclohexanediamine deriv. (III): III.HCl showed IC<sub>50</sub> of 1.2 nM against human factor Xa.

IT 480448-97-3P

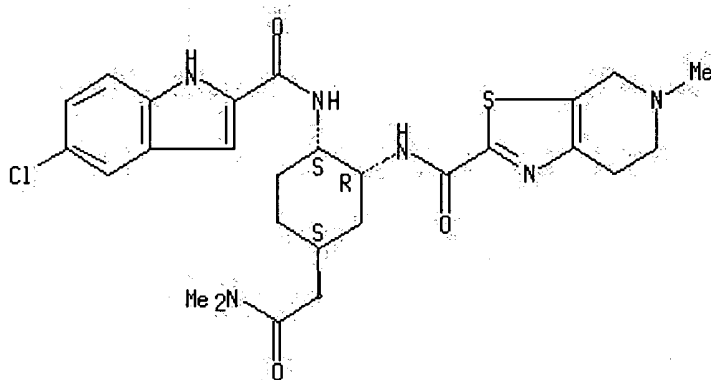
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N,N'-bis(heterocyclic acyl)cycloalkanediamine and heterocyclolediamine derivs. as factor Xa and blood coagulation inhibitors for prevention and treatment of thrombus and embolism)

RN 480448-97-3 HCAPLUS

CN Thiazolo[5,4-c]pyridine-2-carboxamide, N-[(1R,2S,5S)-2-[[5-chloro-1H-indol-2-yl]carbonyl]amino]-5-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]-4,5,6,7-tetrahydro-5-methyl-, monohydrochloride, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



# HCl

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2001:730696 HCAPLUS  
 DOCUMENT NUMBER: 135:272793  
 TITLE: Preparation of ceramide derivatives for pharmaceutical use as antitumor agents  
 INVENTOR(S): Ali, Shaukat; Tang, Hsin-yi Yvette; Mayhew, Eric; Janoff, Andrew B.  
 PATENT ASSIGNEE(S): The Liposome Company, Inc., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072701	A1	20011004	WO 2001-US9894	20010328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1268414	A1	20030102	EP 2001-928328	20010328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003528851	T2	20030930	JP 2001-570614	20010328
PRIORITY APPLN. INFO.:			US 2000-192719P	P 20000328
			WO 2001-US9894	W 20010328

OTHER SOURCE(S): MARPAT 135:272793

AB A ceramides, such as R-A-CH(OH)CH(CH<sub>2</sub>OH)NH-M-Q(X)(Y)Z [R = C1-18-alkyl; A = -(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>CH(OH)-, CH:CH; M = CO, CH<sub>2</sub>; Q = C, CO, SO<sub>2</sub>N; X = F, Cl, Br, I, Ph, OSiMe<sub>3</sub>, OSiBu<sub>3</sub>, OSiPh<sub>3</sub>, alkyl, etc.; Y = H, OH, CO<sub>2</sub>H, Ph, NH<sub>2</sub>, NO<sub>2</sub>, alkyl, aryl, halogen, etc.; Z = H, Ph, NH<sub>2</sub>, CO<sub>2</sub>H, alkyl, etc.], were prepd. for use as antitumor agents. Thus, Sphingosine was N-acylated with



bromoacetic acid using 1,3-dicyclohexylcarbodiimide and Et<sub>2</sub>N in anhyd. CH<sub>2</sub>Cl<sub>2</sub> to give N-(bromoacetyl)sphingosine. The prepd. ceramides were extensively tested for antitumor activity and antitumor structure-activity relationships.

## IT 363183-19-1P

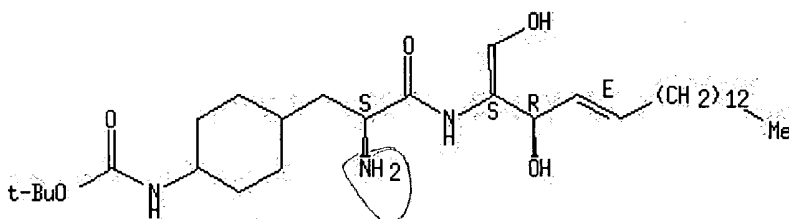
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-acylceramides for pharmaceutical use as antitumor agents)

RN 363183-19-1 HCAPLUS

CN Carbamic acid, [4-[(2S)-2-amino-3-[[[(1S,2R,3E)-2-hydroxy-1-(hydroxymethyl)-3-heptadecenyl]amino]-3-oxopropyl]cyclohexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER:

2001:334117 HCAPLUS

DOCUMENT NUMBER:

135:133802

TITLE:

Synthesis and hydrolysis by cathepsin B of fluorogenic substrates with the general structure benzoyl-X-ARG-MCA containing non-natural basic amino acids at position X

AUTHOR(S):

Melo, R. L.; Barbosa Pozzo, R. C.; Alves, L. C.; Perissutti, E.; Caliendo, G.; Santagada, V.; Juliano, L.; Juliano, M. A.

CORPORATE SOURCE:

Department of Biophysics, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, 04044-020, Brazil

SOURCE:

Biochimica et Biophysica Acta (2001), 1547(1), 82-94  
CODEN: BBACQ; ISSN: 0006-3002

PUBLISHER:

Elsevier Science B.V.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

OTHER SOURCE(S):

CASREACT 135:133802

AB We synthesized one series of fluorogenic substrates for cathepsin B derived from the peptide Bz-F-R-MCA (Bz = benzoyl, MCA = 7-methyl-coumarin amide) substituting Phe at the P2 position by non-natural basic amino acids that combine a pos. charged group with arom. or aliph. radicals at the same side chain, namely, 4-aminomethyl-phenylalanine, 4-guanidine-phenylalanine, 4-aminomethyl-N-isopropyl-phenylalanine, 3-pyridyl-alanine, 4-piperidinyl-alanine, 4-aminomethyl-cyclohexyl-alanine, 4-aminocyclohexyl-alanine, and Nim-dimethyl-histidine. Bz-F-R-MCA was the best substrate for cathepsin B but it also hydrolyzed Bz-R-R-MCA with lower efficiency, since the protease accepts Arg at S2 due to the presence of Glu245 at the bottom of this subsite. The presence of

the basic non-natural amino acids at the P2 position of the substrate partially restored the catalytic efficiency of cathepsin B. All the kinetic parameters for hydrolysis of the peptides described in this paper are in accordance with the structures of the S2 pocket previously described. In addn., the substrate with 4-aminocyclohexyl-alanine presented the highest affinity to cathepsin B although the peptide was obtained from a mixt. of cis/trans isomers of the amino acid and we were not able to sep. them. For comparison all the obtained substrates were assayed with cathepsin L and papain.

## IT 343306-14-9P

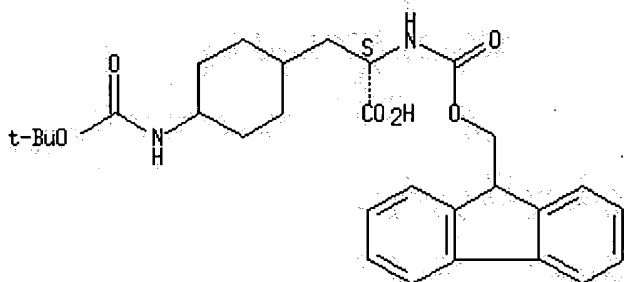
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and hydrolysis by cathepsin B of fluorogenic substrates with the general structure benzoyl-X-ARG-MCA contg. non-natural basic amino acids at position X)

RN 343306-14-9 HCAPLUS

CN Cyclohexanepropanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -[[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



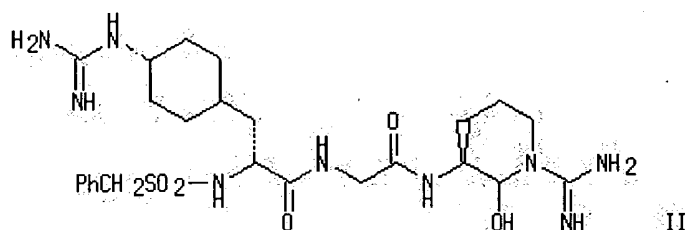
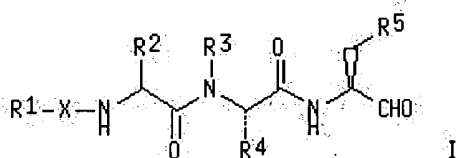
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 2001:283983 HCAPLUS  
 DOCUMENT NUMBER: 134:311435  
 TITLE: Preparation of inhibitors of factor Xa having an arginine or arginine aldehyde mimic  
 INVENTOR(S): Semple, Joseph Edward; Brunck, Terence Kevin; Levy, Odile Esther; Tamura, Susan Y.  
 PATENT ASSIGNEE(S): Corvas International, Inc., USA  
 SOURCE: PCT Int. Appl., 163 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

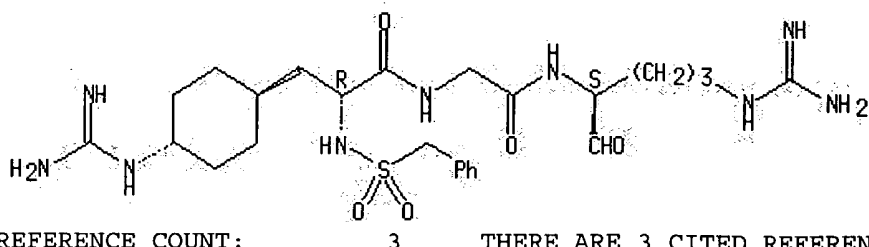
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027141	A1	20010419	WO 2000-US27615	20001006
W: CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.:		US 1999-414903		A 19991008
OTHER SOURCE(S):		MARPAT 134:311435		



IT 334953-07-0P

RN 334953-07-0 HCAPLUS

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

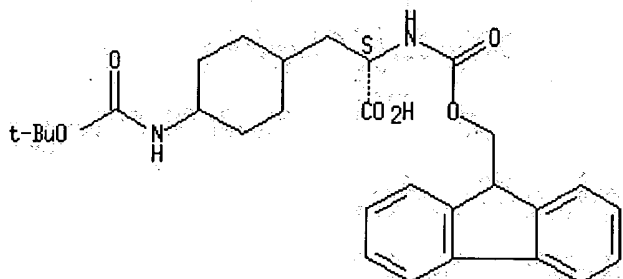
ACCESSION NUMBER: 2001:234536 HCAPLUS  
 DOCUMENT NUMBER: 135:15905  
 TITLE: Human Tissue Kallikrein S1 Subsite Recognition of Non-Natural Basic Amino Acids  
 AUTHOR(S): Melo, Robson L.; Pozzo, Roseli C. Barbosa; Pimenta, Daniel C.; Perissutti, Elisa; Caliendo, Giuseppe; Santagada, Vincenzo; Juliano, Luiz; Juliano, Maria A.  
 CORPORATE SOURCE: Departamento de Biofisica, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, 04044-020, Brazil  
 SOURCE: Biochemistry (2001), 40(17), 5226-5232  
 CODEN: BICHAW; ISSN: 0006-2960  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 135:15905

AB We explored the unique substrate specificity of the primary S1 subsite of human urinary kallikrein (hK1), which accepts both Phe and Arg, using internally quenched fluorescent peptides Abz-F-X-S-R-Q-EDDnp and Abz-G-F-S-P-F-X-S-S-R-P-Q-EDDnp [Abz is o-aminobenzoic acid; EDDnp is N-(2,4-dinitrophenyl)ethylenediamine], which were based on the human kininogen sequence at the C-terminal region of bradykinin. Position X, which in natural sequence stands for Arg, was replaced by the following synthetic basic non-natural amino acids: 4-(aminomethyl)phenylalanine (Amf), 4-guanidine phenylalanine (Gnf), 4-(aminomethyl)-N-isopropylphenylalanine (Iaf), Nim-(dimethyl)histidine [H(2Me)], 3-pyridylalanine (Pya), 4-piperidylalanine (Ppa), 4-(aminomethyl)cyclohexylalanine (Ama), and 4-(aminocyclohexyl)alanine (Aca). Only Abz-F-Amf-S-R-Q-EDDnp and Abz-F-H(2Me)-S-R-Q-EDDnp were efficiently hydrolyzed, and all others were resistant to hydrolysis. However, Abz-F-Ama-S-R-Q-EDDnp inhibited hK1 with a  $K_i$  of 50 nM with high specificity compared to human plasma kallikrein, thrombin, plasmin, and trypsin. The Abz-G-F-S-P-F-X-S-S-R-P-Q-EDDnp series were more susceptible to hK1, although the peptides with Gnf, Pya, and Ama were resistant to it. Unexpectedly, the peptides in which X is His, Lys, H(2Me), Amf, Iaf, Ppa, and Aca were cleaved at amino or at carboxyl sites of these amino acids, indicating that the S1' subsite has significant preference for basic residues. Human plasma kallikrein did not hydrolyze any peptide of this series except the natural sequence where X is Arg. In conclusion, the S1 subsite of hK1 accepts amino acids with combined basic and arom. side chain, although for the S1-P1 interaction the preference is for aliph. and basic side chains.

IT 343306-14-9P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (human tissue kallikrein S1 displays subsite recognition of non-natural basic amino acids)

RN 343306-14-9 HCAPLUS  
 CN Cyclohexanepropanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]- $\alpha$ -  
 [[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-, ( $\alpha$ S)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
 Text References

ACCESSION NUMBER: 2001:137020 HCAPLUS  
 DOCUMENT NUMBER: 134:193741  
 TITLE: Preparation of peptide derivatives as cell adhesion inhibitors  
 INVENTOR(S): Lee, Wen-Cherng; Scott, Daniel; Cornebise, Mark; Petter, Russell  
 PATENT ASSIGNEE(S): Biogen, Inc., USA  
 SOURCE: PCT Int. Appl., 144 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012186	A1	20010222	WO 2000-US22285	20000814
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013248	A	20020723	BR 2000-13248	20000814
EP 1265606	A1	20021218	EP 2000-959232	20000814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003506491	T2	20030218	JP 2001-516532	20000814
EE 200200070	A	20030415	EE 2002-70	20000814
US 6630503	B1	20031007	US 2000-638652	20000814
NZ 517011	A	20040227	NZ 2000-517011	20000814
ZA 2002001158	A	20030512	ZA 2002-1158	20020211
NO 2002000725	A	20020408	NO 2002-725	20020213
BG 106510	A	20021031	BG 2002-106510	20020311

PRIORITY APPLN. INFO.:

US 1999-148845P P 19990813

WO 2000-US22285 W 20000814

OTHER SOURCE(S): MARPAT 134:193741

AB Cell adhesion inhibitors of the general formula R3-L-L'-R1 (R1 = H, C1-10alkyl, C2-10alkenyl or -alkynyl, cycloalkyl, cycloalkylalkyl, -alkenyl, or -alkynyl; L' and L are hydrocarbon linker moieties having 1-5 or 1-14 carbons, resp., which are optionally substituted and interrupted by, or terminally attached to, various groups; R3 = alkyl, cycloalkyl, aryl, aralkyl, aryloxy, arylamino, heterocyclyl, etc.) were prepd. An inhibitor of the present invention interacts with VLA-4 mols. to inhibit VLA-4 dependent cell adhesion. Thus, N2-[N-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl]-N4-[N-(o-MePUPA)-N-methyl-L-leucyl]-L-2,4-diaminobutyric acid [o-MePUPA = 4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl] was prepd. via peptide coupling reactions in soln.

IT 327621-85-2P

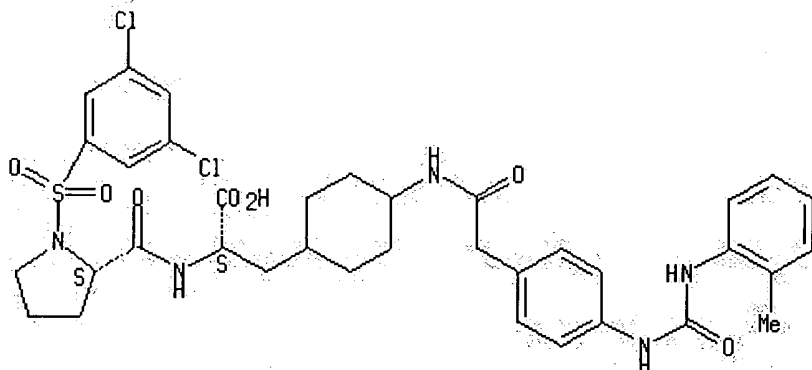
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptide derivs. as cell adhesion inhibitors)

RN 327621-85-2 HCAPLUS

CN L-Alanine, 1-[(3,5-dichlorophenyl)sulfonyl]-L-prolyl-3-[4-[[[4-[[[(2-methylphenyl)amino]carbonyl]amino]phenyl]acetyl]amino]cyclohexyl]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
TextCiting  
References

ACCESSION NUMBER:

2001:118603 HCAPLUS

DOCUMENT NUMBER:

134:326510

TITLE:

Potent and selective bicyclic lactam inhibitors of thrombin. Part 4: transition state inhibitors

AUTHOR(S):

Bachand, B.; Tarazi, M.; St. Denis, Y.; Edmunds, J. J.; Winocour, P. D.; Leblond, L.; Siddiqui, M. A.

CORPORATE SOURCE:

BioChem Pharma Inc., Laval, QC, H7V 4A7, Can.

SOURCE:

Bioorganic & Medicinal Chemistry Letters (2001), 11(3), 287-290

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER:

Elsevier Science Ltd.

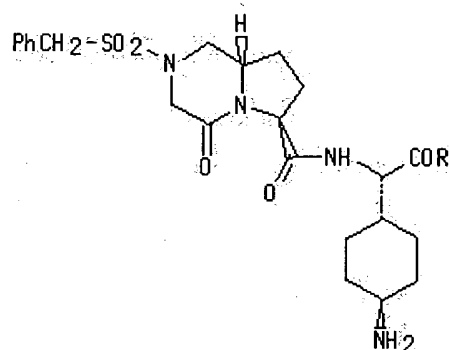
DOCUMENT TYPE:

Journal

LANGUAGE:

English

GI



AB Title compds. I (R = 2-thiazolyl, 2-benzothiazolyl, CONHMe, CO<sub>2</sub>Me, CO<sub>2</sub>H, CO<sub>2</sub>Bu, COSEt, CONHCH<sub>2</sub>CO<sub>2</sub>H, 1-methyltetrazolyl, etc.) were prepd. as thrombin inhibitors and were evaluated in vitro and in vivo. I, having in common an electrophilic basic trans-cyclohexylamine P1 residue, displayed high thrombin affinity, high selectivity against trypsin and good in vivo efficacy in the rat arterial thrombosis model.

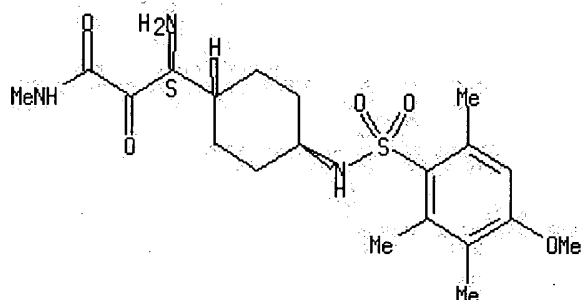
IT **209796-59-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of bicyclic lactams as potent and selective inhibitors of thrombin)

RN **209796-59-8** HCAPLUS

CN Cyclohexanepropanamide, β-amino-4-[[[4-methoxy-2,3,6-trimethylphenyl)sulfonyl]amino]-N-methyl-α-oxo-, monohydrochloride, (βS,trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



# HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1999:764071 HCAPLUS  
DOCUMENT NUMBER: 132:23191  
TITLE: Preparation of peptide antiangiogenic drugs  
INVENTOR(S): Henkin, Jack; Haviv, Fortuna; Bradley, Michael F.;  
Kalvin, Douglas M.; Schneider, Andrew J.  
PATENT ASSIGNEE(S): Abbott Laboratories, USA  
SOURCE: PCT Int. Appl., 223 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961476	A1	19991202	WO 1999-US11448	19990521
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2329250	AA	19991202	CA 1999-2329250	19990521
AU 9944075	A1	19991213	AU 1999-44075	19990521
AU 764277	B2	20030814		
EP 1078002	A1	20010228	EP 1999-927091	19990521
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
BR 9910639	A	20020115	BR 1999-10639	19990521
JP 2002516342	T2	20020604	JP 2000-550879	19990521
NZ 507912	A	20021025	NZ 1999-507912	19990521
NO 2000005890	A	20010112	NO 2000-5890	20001121
BG 105064	A	20010831	BG 2000-105064	20001218

## PRIORITY APPLN. INFO.:

US 1998-83745	A	19980522
US 1999-250574	A	19990216
US 1999-277466	A	19990326
WO 1999-US11448	W	19990521

## OTHER SOURCE(S): MARPAT 132:23191

AB Peptides A0-A1-A2-A3-A4-A5-A6-A7-A8-A9-A10 (A0 is H or an acyl group; A10 is OH or an amino acid amide; A1-9 are amino acyl residues) or their pharmaceutically acceptable salts, esters, solvates, or prodrugs were prepd. for the treatment of angiogenesis. Thus, N-Ac-Sar-Gly-Val-D-Ile-Thr-Nva-Ile-Arg-Pro-NHET was prepd. by the solid-phase method and assayed for in vitro angiogenic activity (87.3% at 20 nM and 76.9 at 10 nM).

## IT 251900-41-1P

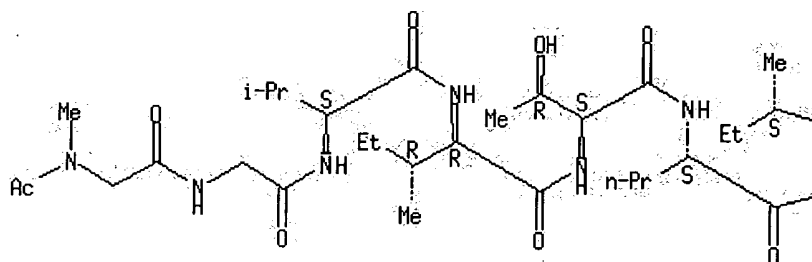
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of peptide antiangiogenic drugs)

## RN 251900-41-1 HCAPLUS

CN L-Prolinamide, N-acetyl-N-methylglycylglycyl-L-valyl-D-isoleucyl-L-threonyl-L-norvalyl-L-isoleucyl-3-[4-[(1-methylethyl)amino]cyclohexyl]-L-alanyl-N-ethyl- (9CI) (CA INDEX NAME)

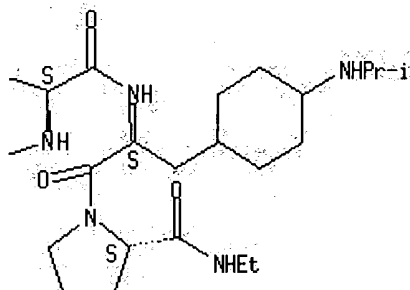
Absolute stereochemistry.

PAGE 1-A





PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

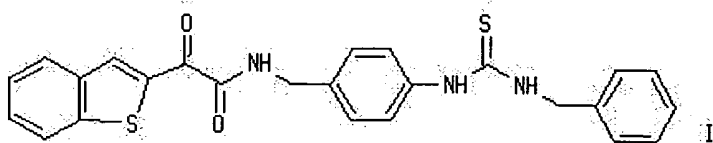
ACCESSION NUMBER: 1998:706197 HCAPLUS  
DOCUMENT NUMBER: 129:275833  
TITLE: Combinatorial synthesis and screening of  $\alpha$ -ketoamide-derivative cysteine protease inhibitors  
INVENTOR(S): Blandino, Carmen M.; Coffen, David L.; Chipman, Stewart D.; Cheng, Hong  
PATENT ASSIGNEE(S): Arqule, Inc., USA  
SOURCE: PCT Int. Appl., 71 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846559	A1	19981022	WO 1998-US7747	19980416
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9871290	A1	19981111	AU 1998-71290	19980416
EP 975584	A1	20000202	EP 1998-918344	19980416
EP 975584	B1	20020925		

R: CH, DE, DK, FR, GB, IT, LI, NL, SE

PRIORITY APPLN. INFO.: US 1997-843584 A 19970416  
WO 1998-US7747 W 19980416

OTHER SOURCE(S): MARPAT 129:275833  
GI



AB Via combinatorial synthesis, about 38,000  $\alpha$ -ketoamide derivs. were prepd. and the arrays screened, from which 6 compds. were isolated which had a high inhibitory activity against three cysteine proteases: cruzain, papain, and cathepsin B; these title compds. may be useful in the treatment of diseases (e.g., Chagas' disease) assocd. with these proteases. Thus, Me 2-(2-benzothieryl)-2-oxoethanoate was amidated with 4-aminobenzyl amine, the intermediate isolated and reacted with benzyl isothiocyanate, producing ther 2-benzothieryl  $\alpha$ -ketoamide I which demonstrated an IC<sub>50</sub> for cruzain of 2.2  $\mu$ M and 3.3  $\mu$ M for cathepsin B.

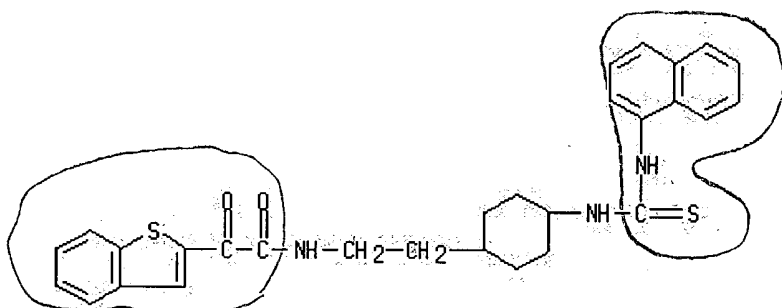
IT **214061-03-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(combinatorial synthesis and screening of benzothiophene  $\alpha$ -ketoamide-deriv. cysteine protease inhibitors)

RN 214061-03-7 HCAPLUS

CN Benzo[b]thiophene-2-acetamide, N-[2-[4-[(1-naphthalenylamino)thioxomethyl]amino]cyclohexyl]ethyl]- $\alpha$ -oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

12

THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER:

1998:479552 HCAPLUS

DOCUMENT NUMBER:

129:109333

TITLE:

Preparation of heterobicyclic peptide derivatives as thrombin inhibitors

INVENTOR(S):

Bachand, Benoit; Doherty, Annette Marian; Siddiqui, M. Arshad; Edmunds, Jeremy John

PATENT ASSIGNEE(S):

Biochem Pharma Inc., Can.

SOURCE:

PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

WO 9828326 A1 19980702 WO 1997-US22985 19971222

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
 DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,  
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,  
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
 GA, GN, ML, MR, NE, SN, TD, TG

AU 9855260 A1 19980717 AU 1998-55260 19971222

PRIORITY APPLN. INFO.:

US 1996-34311P P 19961223

WO 1997-US22985 W 19971222

OTHER SOURCE(S): MARPAT 129:109333

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB This invention relates to heterobicyclic peptide derivs. I [A = (CHR8)0-1, S, S(O), SO<sub>2</sub>, NR<sub>8</sub>; B = S, SO<sub>2</sub>, O, N, NH, CH, CR<sub>6</sub>R<sub>7</sub>; D = (CHR9)0-2, CH; E = CH<sub>2</sub>, CHCOR<sub>9</sub>; X = O, NR<sub>5</sub>, CHR<sub>5</sub>; Y = O, S, S(O), SO<sub>2</sub>, NR<sub>5</sub>, CO, CHR<sub>8</sub>; Z = O, S, H<sub>2</sub>; R<sub>1</sub> = any group Q-Q<sub>3</sub>; J = CH, N; K = bond, NH, G = C<sub>1</sub>-4 alkoxy, CN, NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, C(NH<sub>2</sub>):NH, NHC(NH<sub>2</sub>):NH, CH<sub>2</sub>NHC(NH<sub>2</sub>):NH, etc; U = CN, NH<sub>2</sub>, C(NH<sub>2</sub>):NH, NHC(NH<sub>2</sub>):NH; T = H, OH, amino, peptide residue contg. 1-4 amino acids, C<sub>1</sub>-6 alkyl, C<sub>1</sub>-16 alkoxy, C<sub>6</sub>-20 aralkyl, C<sub>6</sub>-16 aryloxy, C<sub>6</sub>-20 arylalkoxy, (un)substituted aryl or heterocycle; R<sub>2</sub> = H, (un)substituted C<sub>1</sub>-6 alkyl; R<sub>3</sub> = H, NR<sub>6</sub>R<sub>7</sub>, C<sub>1</sub>-6 alkyl; R<sub>4</sub>, R<sub>5</sub> = independently H, NR<sub>6</sub>R<sub>7</sub>, C<sub>6</sub>-16 aryl, (un)substituted C<sub>3</sub>-7 cycloalkyl, (un)substituted, optionally heteroatom-interrupted C<sub>1</sub>-6 alkyl; R<sub>6</sub>, R<sub>7</sub> = independently H, C<sub>1</sub>-6 alkyl; R<sub>8</sub> = H, optionally heteroatom-interrupted C<sub>1</sub>-6 alkyl, C<sub>6</sub>-16 aryl, C<sub>3</sub>-7 cycloalkyl, heterocyclyl, hydrophobic group; R<sub>9</sub> = H, C<sub>1</sub>-6 alkyl, COR<sub>1</sub>; R<sub>11</sub> = H, C<sub>1</sub>-6 alkyl], their prepn., and pharmaceutical compns. thereof, as thrombin inhibitors. Also, the invention relates to the use of such compds. and compns. as anticoagulants and as agents for the treatment and prophylaxis of thrombotic disorders such as venous thrombosis, pulmonary embolism and arterial thrombosis resulting in acute ischemic events such as myocardial infarction or cerebral infarction. Thus, amidation of keto ester II (Mtr = 4-methoxy-2,3,6-trimethylbenzenesulfonyl) (prepn. given) with octahydropyrrolo[1,2-a]pyrazinecarboxylic acid III, followed by sapon. and acidic deprotection gave inhibitor IV as a trifluoroacetate salt. IV inhibited human  $\alpha$ -thrombin with K<sub>i</sub> = 0.09 nM in an in vitro assay.

IT 209796-58-7P

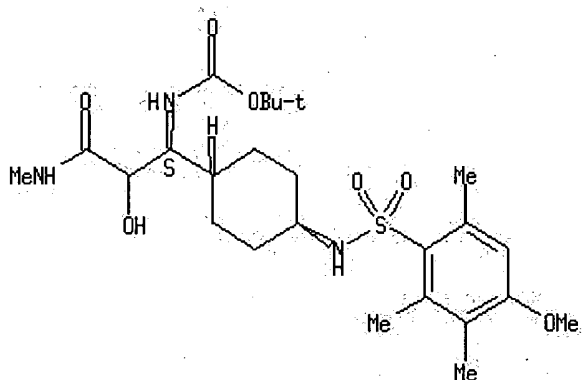
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of heterobicyclic peptide derivs. as thrombin inhibitors)

RN 209796-58-7 HCAPLUS

CN Carbamic acid, [(1S)-2-hydroxy-1-[trans-4-[[[4-methoxy-2,3,6-trimethylphenyl)sulfonyl]amino]cyclohexyl]-3-(methylamino)-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1997:640243 HCAPLUS  
DOCUMENT NUMBER: 127:293641  
TITLE: Preparation of peptidyl cyclohexylamines as thrombin inhibitors  
INVENTOR(S): Veber, Daniel F.; Lewis, S. Dale; Shafer, Jules A.; Feng, Dong-mei; Nutt, Ruth F.; Brady, Stephen F.  
PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 55,611, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5672582	A	19970930	US 1994-322049	19941012
CA 2159834	AA	19941110	CA 1994-2159834	19940425
ES 2184763	T3	20030416	ES 1994-915883	19940425
WO 9611697	A1	19960425	WO 1995-US13220	19951006

W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ

RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9538328	A1	19960506	AU 1995-38328	19951006
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PRIORITY APPLN. INFO.:	US 1993-55611	B2	19930430
	US 1994-322049	A1	19941012
	WO 1995-US13220	W	19951006

OTHER SOURCE(S): MARPAT 127:293641

AB Peptidyl cyclohexylamine derivs. RR1NCHR3C(Z)NR1CHR4(CR1R2)mC6H10NH2-4 [C6H10 is a cyclohexane ring, R = arylsulfonyl, substituted acyl or 1-carboxyalkyl; R1, R2 = H, Me; R3 = H, (un)substituted alkyl or aryl, arylmethyl, cycloalkylmethyl, cycloalkyl or R1R3 = (CH2)n (n = 2-4); R4 = (un)substituted carbamoyl, carbalkoxycarbonyl, etc.; Z = O or H2; m = 0, 1] were prepd. as thrombin inhibitors. Thus, MeNH-D-Phe-Pro-NH-DL-CH(COCO2H)C6H10NH2-4 was prepd. and shown to inhibit thrombin selectively (Ki = 0.05  $\mu$ M vs. 51  $\mu$ M for trypsin).

IT 197227-37-5P

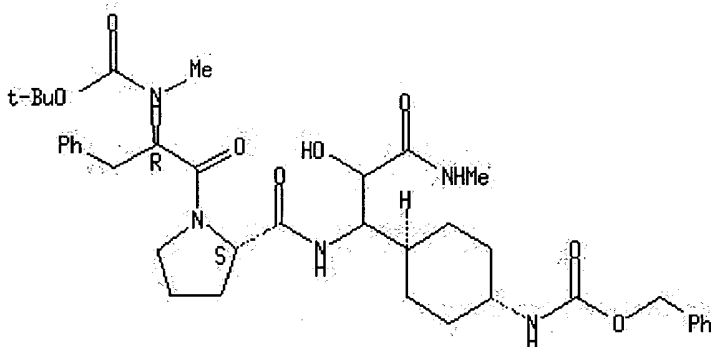
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of peptidyl cyclohexylamines as thrombin inhibitors)

RN 197227-37-5 HCAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-D-phenylalanyl-L-prolyl-2-hydroxy-N-methyl-3-[trans-4-[[[(phenylmethoxy)carbonyl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 17 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1997:594514 HCAPLUS  
 DOCUMENT NUMBER: 127:234621  
 TITLE: Amidino and guanidino substituted boronic acid inhibitors of trypsin-like enzymes  
 INVENTOR(S): Lee, Sheng-lian O.; Carini, David John; Fevig, John Matthew; Kettner, Charles Adrian; Mantri, Padmaja; Feng, Zixia  
 PATENT ASSIGNEE(S): Dupont Merck Pharmaceutical Co., USA  
 SOURCE: U.S., 45 pp., Cont.-in-part of U. S. Ser. No. 204,055, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5658885	A	19970819	US 1994-329039	19941025
ZA 9402899	A	19951026	ZA 1994-2899	19940426
CA 2200192	AA	19960502	CA 1995-2200192	19951024
CA 2200192	C	20010116		
WO 9612499	A1	19960502	WO 1995-US13702	19951024
W: AU, CA, JP, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9539671	A1	19960515	AU 1995-39671	19951024
EP 787010	A1	19970806	EP 1995-937612	19951024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10508010	T2	19980804	JP 1995-514116	19951024
PRIORITY APPLN. INFO.:				
			US 1993-52835	B2 19930427
			US 1994-204055	B2 19940302
			US 1994-329039	A 19941025
			WO 1995-US13702	W 19951024

OTHER SOURCE(S): MARPAT 127:234621

AB Title boronic acids R3XnNR2CHR1BR4R5 [X = amino acid or peptide residue; n = 0, 1; R1 = guanidino- or aminoxy-substituted alkyl, substituted Ph, phenylalkyl, cycloalkyl, or cycloalkylalkyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, alkylaryl; R3 = H, alkyl, aryl, alkylaryl, NH2 blocking group, etc.; R4, R5 = OH or taken together form a cyclic boronate ester] were prepd. as inhibitors of trypsin-like enzymes. Thus, Ac-D-Phe-Pro-NHCH[(CH2)4CN]BO2C10H16 was prepd. by coupling of Ac-D-Phe-Pro-OH with H2N-CH[(CH2)4Br]BO2C10H16.HCl, followed by cyanation. The product inhibited thrombin with Ki of <50,000 nM.

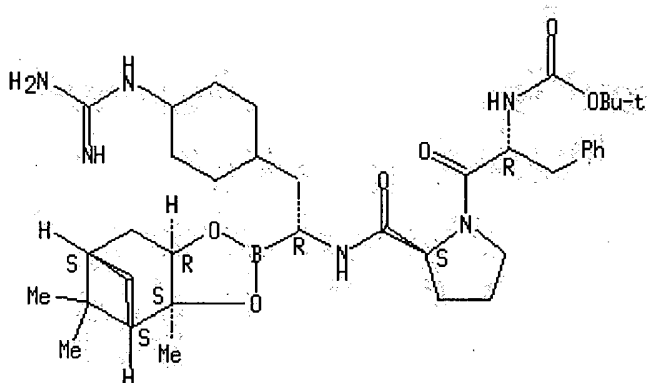
IT **194987-72-9P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(amidino and guanidino substituted boronic acid inhibitors of trypsin-like enzymes)

RN **194987-72-9** HCAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-N-[(1R)-2-[4-[(aminoiminomethyl)amino]cyclohexyl]-1-[(3aS,4S,6S,7aR)-hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 18 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1997:570901 HCAPLUS  
DOCUMENT NUMBER: 127:205897  
TITLE: Antagonists of LHRH  
INVENTOR(S): Bowers, Cyril Y.; Folkers, Karl A.; Janecka, Anna  
PATENT ASSIGNEE(S): Administrators of the Tulane Educational Fund, USA;  
Board of Regents, University of Texas System  
SOURCE: U.S., 7 pp., Cont.-in-part of U. S. 5,480,969.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5656727	A	19970812	US 1995-430602	19950428
US 5480969	A	19960102	US 1992-946056	19920915
CA 2219263	AA	19961031	CA 1996-2219263	19960426
WO 9633729	A1	19961031	WO 1996-US5682	19960426

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,

ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,  
LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
SG, SI

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML

AU 9656670 A1 19961118 AU 1996-56670 19960426

AU 703400 B2 19990325

EP 822827 A1 19980211 EP 1996-913829 19960426

EP 822827 B1 20030305

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

JP 11504335 T2 19990420 JP 1996-532655 19960426

AT 233567 E 20030315 AT 1996-913829 19960426

PT 822827 T 20030731 PT 1996-96913829 19960426

ES 2191753 T3 20030916 ES 1996-913829 19960426

PRIORITY APPLN. INFO.:

US 1992-946056 A2 19920915

US 1995-430602 A 19950428

WO 1996-US5682 W 19960426

AB LHRH analogs and congeners with high water soly. have been synthesized. Thus, (NacDQal1, DPtf2, DPal3, cisPzACAla5, DPicLys6, DALa10)LHRH [NacDQal = N-acetyl-3-(3-quinolyl)alanine, Ptf = 3-[4-(trifluoromethyl)phenyl]alanine, Pal = 3-(3-pyridyl)alanine, Pz = pyrazinecarboxylic acid, ACAla = 4-aminocyclohexylalanine, PicLys = N $\epsilon$ -picolinoyllysine] was prepd. by the solid-phase method. This peptide had 100% antioviulatory activity at a 0.25  $\mu$ g dosage and the ED50 for histamine release was 40  $\mu$ g/mL.

IT 137584-28-2P

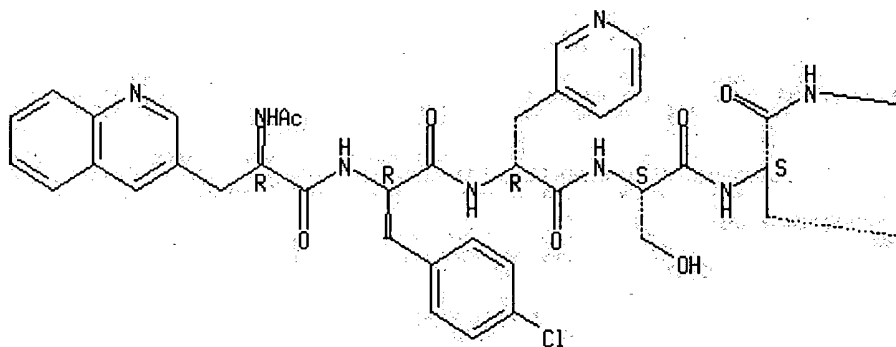
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(antagonists of LHRH)

RN 137584-28-2 HCAPLUS

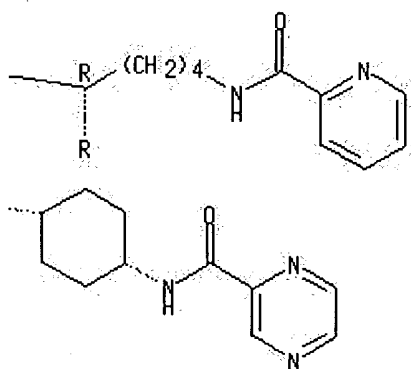
CN D-Alaninamide, N-acetyl-3-(3-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

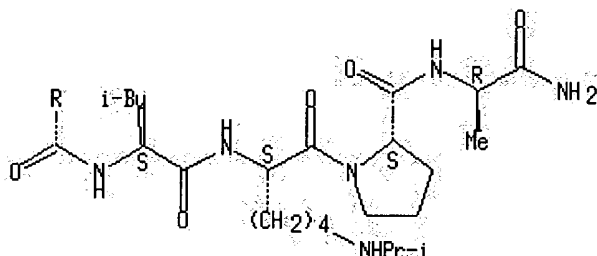
PAGE 1-A



PAGE 1-B



PAGE 2-A



L8 ANSWER 19 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1997:151012 HCAPLUS  
 DOCUMENT NUMBER: 126:324952  
 TITLE: Synthesis and evaluation of antitumor activity of arylamides and cyclohexylamides of isomeric 3-chloro-4-(2-chloroethylthio)butanoic- and 4-chloro-3-(2-chloroethylthio)butanoic acids  
 AUTHOR(S): Vektariene, Ausra; Palaima, Algirdas; Simkeviciene, Vitalija  
 CORPORATE SOURCE: Department Patent Analysis Scientific Information, Institute Biochemistry, Vilnius, 2600, Lithuania  
 SOURCE: Arzneimittel-Forschung (1997), 47(2), 217-222  
 CODEN: ARZNAD; ISSN: 0004-4172  
 PUBLISHER: Cantor  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Among bis(2-chloroethyl) sulfides only 3-chloro-4-(2-chloroethylthio)butanoic (3-chloro) and 4-chloro-3-(2-chloroethylthio)butanoic (4-chloro) acids possessed definite alkylating ability. However, the clin. use of these agents is hampered by their high toxicity. A no. of arylamides and cyclohexyl-amides of 3-chloro and 4-chloro acids were synthesized. A study of the toxicity and antitumor activity of synthesized derivs. in comparison with known 4-chloro-3-(2-chloroethylthio)butanoic acids showed that both 3-chloro and 4-chloro isomers possessed high antitumor activity. Substitution of 3-chloro and 4-chloro butanoic acids by arylamides and cyclohexylamides residues R did not increase the antitumor activity of the compds. The presence of an anilide and cyclohexylamide carboxylic or alkylencarboxylic substituent reduced the toxicity of the compds. 3-5 times in comparison with 3-chloro and 4-chloro anilides and



cyclohexylamides. All synthesized compds. possessed a broad spectrum of antitumor activity and were less toxic than the parent compd.  
4-chloro-3-(2-chloroethylthio)butanoic acid.

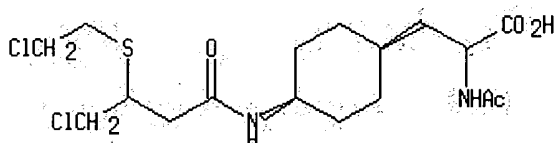
IT 189504-72-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. and antitumor activity of arylamides and cyclohexylamides of isomeric chloro butanoic acids)

RN 189504-72-1 HCAPLUS

CN Cyclohexanepropanoic acid,  $\alpha$ -(acetylamino)-4-[[4-chloro-3-[(2-chloroethyl)thio]-1-oxobutyl]amino]-, (1 $\alpha$ ,4 $\alpha$ )-[partial]- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



L8 ANSWER 20 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1997:12601 HCAPLUS  
DOCUMENT NUMBER: 126:43159  
TITLE: Antagonists of LH-RH  
INVENTOR(S): Bowers, Cyril Y.; Folkers, Karl A.; Janecka, Anna  
PATENT ASSIGNEE(S): University of Texas System, USA; The Administrators of the Tulane Educational Fund  
SOURCE: PCT Int. Appl., 16 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633729	A1	19961031	WO 1996-US5682	19960426
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5656727	A	19970812	US 1995-430602	19950428
AU 9656670	A1	19961118	AU 1996-56670	19960426
AU 703400	B2	19990325		
EP 822827	A1	19980211	EP 1996-913829	19960426
EP 822827	B1	20030305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504335	T2	19990420	JP 1996-532655	19960426
AT 233567	E	20030315	AT 1996-913829	19960426
PRIORITY APPLN. INFO.:				
			US 1995-430602	A 19950428
			US 1992-946056	A2 19920915

WO 1996-US5682 W 19960426

AB LHRH analogs and congeners with high water soly. have been synthesized. These new analogs had 0%-100% antiovolatory activity at a 0.5 µg dosage and 0%-80% at 0.25 µg. The ED50 for histamine release was 30.5 µg/mL- > 300 µg/mL.

IT **162412-82-0P**

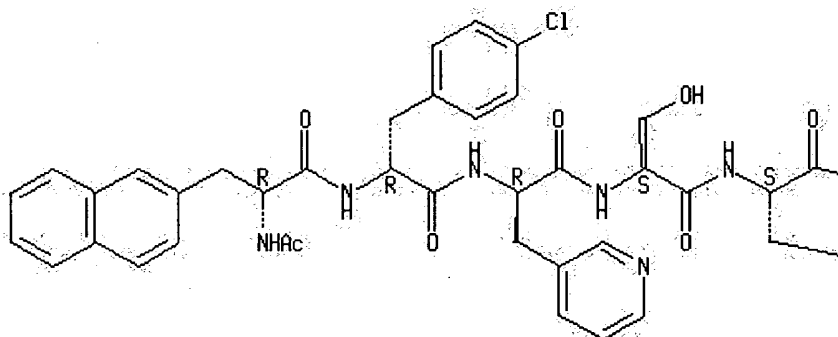
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(antagonists of LH-RH)

RN 162412-82-0 HCAPLUS

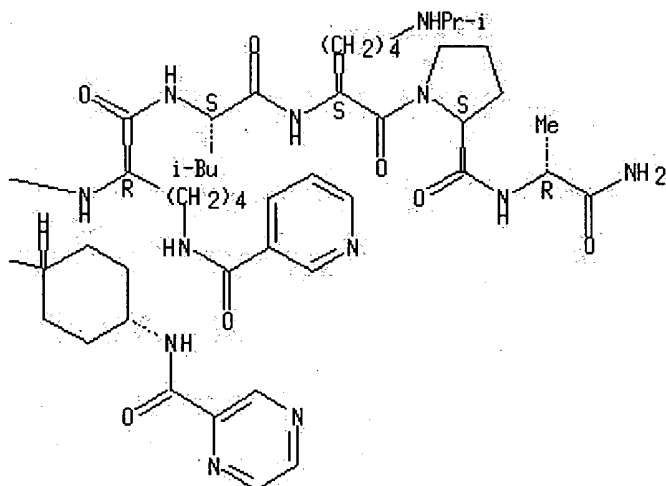
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[cis-4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(3-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L8 ANSWER 21 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1996:509465 HCAPLUS

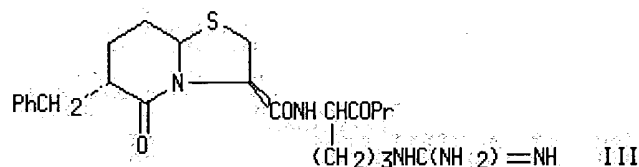
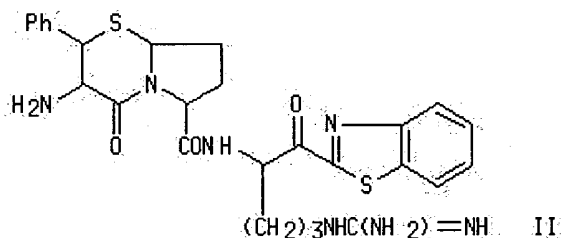
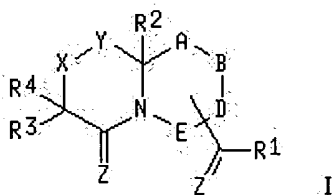
DOCUMENT NUMBER: 125:167970

TITLE: Low molecular weight bicyclic thrombin inhibitors

INVENTOR(S): Dimaio, John; Siddiqui, M. Arshad; Gillard, John W.;

St-Denis, Yves; Tarazi, Micheline; Preville, Patrice;  
 Levesque, Sophie; Bachand, Benoit  
 PATENT ASSIGNEE(S): Biochem Pharma Inc., Can.  
 SOURCE: PCT Int: Appl., 182 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9619483	A1	19960627	WO 1995-CA708	19951221
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2208772	AA	19960627	CA 1995-2208772	19951221
AU 9642505	A1	19960710	AU 1996-42505	19951221
EP 802916	A1	19971029	EP 1995-940923	19951221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
CN 1175259	A	19980304	CN 1995-197614	19951221
HU 77651	A2	19980728	HU 1998-216	19951221
BR 9510433	A	19981110	BR 1995-10433	19951221
NZ 297360	A	20000327	NZ 1995-297360	19951221
AU 9540628	A1	19960704	AU 1995-40628	19951222
AU 715378	B2	20000203		
ZA 9510960	A	19960709	ZA 1995-10960	19951222
ZA 9510961	A	19960709	ZA 1995-10961	19951222
FI 9702466	A	19970819	FI 1997-2466	19970611
NO 9702892	A	19970820	NO 1997-2892	19970620
US 6057314	A	20000502	US 1997-880885	19970623
LV 12019	B	19980720	LV 1997-141	19970715
LT 4368	B	19980825	LT 1997-132	19970721
PRIORITY APPLN. INFO.:			GB 1994-26038	A 19941222
			GB 1995-3136	A 19950217
			GB 1995-10265	A 19950522
			GB 1995-10266	A 19950522
			GB 1995-10267	A 19950522
			WO 1995-CA708	W 19951221
OTHER SOURCE(S):		MARPAT 125:167970		
GI				



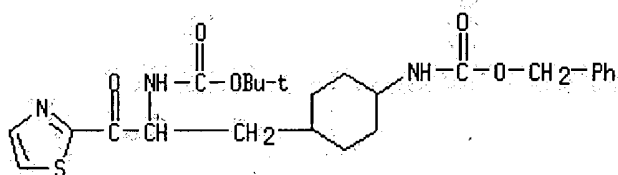
AB Heterobicyclic thrombin inhibitors I (A, B = CH, S, O, etc.; D = CH, C-alkyl, etc.; E = CH<sub>2</sub>, CH-acyl; X = O, NH, etc.; Y = O, S, SO, etc.; Z = O, S, etc.; R1 = e.g., arginyl moiety substituted with an amino acid or heterocycle; R2 = H or organyl; R3 = H, amino, etc.; R4 = H, aryl, cycloalkyl, etc.) were prepd. Thus, benzothiazole deriv. II was prepd. in 7 steps from PhCH<sub>2</sub>SCH<sub>2</sub>CH(NHCBz)COOH and 4-hydroxyproline. In a fibrin clotting assay with human thrombin and bovine fibrinogen, another product (III) showed an IC<sub>50</sub> (concn. required to double the clotting time relative to a control) of 47 μM.

#### IT 180152-05-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(low-mol.-wt. bicyclic thrombin inhibitors)

RN 180152-05-0 HCAPLUS

CN Carbamic acid, [4-[2-[[[(1,1-dimethylethoxy)carbonyl]amino]-3-oxo-3-(2-thiazolyl)propyl]cyclohexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 22 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER:

1996:476626 HCAPLUS

DOCUMENT NUMBER:

125:143313

TITLE:

Preparation of amidino and guanidino substituted peptide analogs as inhibitors of trypsin-like enzymes  
Lee, Sheng-lian O.; Carini, David John; Fevig, John  
Matthew; Kettner, Charles Adrian; Mantri, Padmaja;  
Feng, Zixia

INVENTOR(S):

PATENT ASSIGNEE(S):

Du Pont Merck Pharmaceutical Company, USA

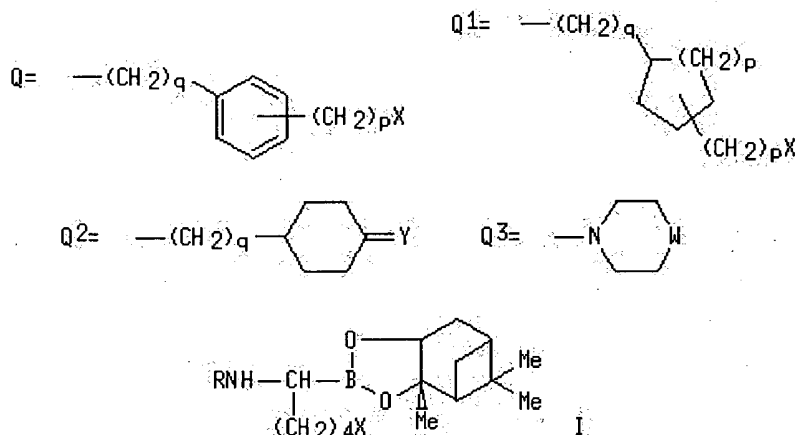
SOURCE:

PCT Int. Appl., 139 pp.

CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612499	A1	19960502	WO 1995-US13702	19951024
W: AU, CA, JP, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5658885	A	19970819	US 1994-329039	19941025
AU 9539671	A1	19960515	AU 1995-39671	19951024
EP 787010	A1	19970806	EP 1995-937612	19951024
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 10508010	T2	19980804	JP 1995-514116	19951024
PRIORITY APPLN. INFO.:				
			US 1994-329039	A 19941025
			US 1993-52835	B2 19930427
			US 1994-204055	B2 19940302
			WO 1995-US13702	W 19951024

OTHER SOURCE(S): MARPAT 125:143313  
 GI



AB Novel  $\alpha$ -amino acid and  $\alpha$ -aminoboronic acid and corresponding peptide analogs of formula R3[A]nNR2CHR1E [E = BY1Y2, COR14, CO2R4, CONR15R16, COR4, COCO2R4; wherein Y1, Y2 = OH, F, (un)substituted NH2; or Y1Y2 = cyclic boron ester, cyclic boron amide, or cyclic boron amide-ester contg. 2-20 carbon atoms and optionally 1-3 heteroatoms selected from N, S, and O; R4 = H, C1-4 alkyl, aryl-C1-4 alkyl, C5-7 cycloalkyl; R14 = CF3, CHF2, CH2F, CH2Cl, CO2R4, CONR15R16, COR4, etc.; R15, R16 = H, C1-4 alkyl, aryl-C1-4 alkyl, C5-7 cycloalkyl, (un)substituted Ph; or NR15R16 = Q3; wherein W = single bond, O, S, SO, SO2, CH2, NR4, NCOR4; R1 = (un)substituted C1-12 alkyl, Q, Q1; wherein X = halo, cyano, NO2, CF3, NH2, NHC(:NH)H, NHC(:NH)NHOH, NHC(:NH)NHCN, etc.; Y = O, :NOH, :NNHCHO; p = 0-3; q = 0-4; R2 = H, (un)substituted C1-12 alkyl, cycloalkyl, Ph, naphthyl, or aryl-C1-4 alkyl; R3 = H, alkyl, aryl, alkylaryl, S(O)rR7, COR7, CO2R7, P(O)2OR7, or any other C1-20 NH2-blocking group; wherein R7 = H, C1-4 alkyl, (un)substituted Ph, naphthyl, or aryl-C1-4 alkyl; r = 0-2; A = amino acid residue or peptide comprised of 2-20 amino acids residue; n = 0,1] and pharmaceutically acceptable salts thereof are prepd. These peptide analogs are useful for treating a physiol. disorder in a warm

blooded animal catalyzed by trypsin-like enzymes, e.g. blood clotting, arterial thrombosis, myocardial infarction, inflammation, pancreatitis, and hereditary angioedema. Trypsin-like enzymes are a group of proteases which hydrolyze peptide bonds at basic residues liberating either a C-terminal arginyl or lysyl residue, among which are enzymes of the blood coagulation and fibrinolytic system required for hemostasis (e.g. factors II, X, VII, IX, kallikrein, tissue plasminogen activators, urokinase-like plasminogen activator, and plasmin), enzymes of the complement system, acrosin, and pancreatic trypsin. Thus, Ac-D-Phe-Pro-OH was condensed with a boronic acid deriv. (I; R = H, X = Br) by a mixed anhydride procedure using iso-Bu chloroformate and N-methylmorpholine in CCl<sub>4</sub> to give an intermediate I (R = Ac-D-Phe-Pro, X = Br), which was heated with Bu<sub>4</sub>NCN in MeCN at 90° for 3 h to give the nitrile I (R = Ac-D-Phe-Pro, X = cyano). The latter nitrile was stirred with satd. methanolic HCl at 4° overnight, concd., and redissolved in MeOH. NH<sub>3</sub>(g) was bubbled through the soln. for 1 h and the soln. was heated at 50° for 3 h to give I [R = Ac-D-Phe-Pro, X = C(:NH)NH<sub>2</sub>]. This compd. in vitro inhibited thrombin with K<sub>i</sub> of <500 nM.

## IT 179614-85-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

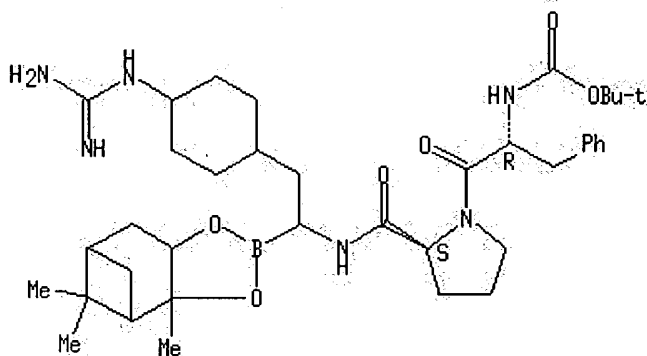
(prepn. of amidino and guanidino substituted peptide analogs contg..

α-aminoboronic acid as inhibitors of trypsin-like enzymes for disease therapy)

RN 179614-85-8 HCAPLUS

CN L-Prolinamide, N-[(1,1-dimethylethoxy)carbonyl]-D-phenylalanyl-N-[2-[4-[(aminoiminomethyl)amino]cyclohexyl]-1-(hexahydro-3a,5,5-trimethyl-4,6-methano-1,3,2-benzodioxaborol-2-yl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 23 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1996:397256 HCAPLUS

DOCUMENT NUMBER: 125:76382

TITLE: Thrombin-inhibiting peptide analogs as anticoagulants

INVENTOR(S): Veber, Daniel F.; Lewis, S. Dale; Shafer, Jules A.; Feng, Dong-mei; Nutt, Ruth F.; Brady, Stephen F.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

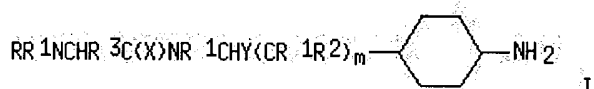
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611697	A1	19960425	WO 1995-US13220	19951006
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5672582	A	19970930	US 1994-322049	19941012
AU 9538328	A1	19960506	AU 1995-38328	19951006
PRIORITY APPLN. INFO.:			US 1994-322049	A1 19941012
			US 1993-55611	B2 19930430
			WO 1995-US13220	W 19951006
OTHER SOURCE(S):			MARPAT 125:76382	
GI				



AB 4-Substituted cyclohexylamine derivs. [I; X = O, H<sub>2</sub>; R = arylsulfonyl, aminoacyl, hydroxyacyl, etc.; R<sub>1</sub>, R<sub>2</sub> = H, Me; R<sub>3</sub> = H, (substituted) C1-3 alkyl, (substituted) aryl, etc.; or R<sub>1</sub>R<sub>3</sub> = (CH<sub>2</sub>)<sub>n</sub>; Y = CHO, C(O)CF<sub>3</sub>, CO<sub>2</sub>R<sub>4</sub>, COCO<sub>2</sub>R<sub>4</sub>, CONR<sub>5</sub>R<sub>6</sub>, etc.; R<sub>4</sub>-R<sub>6</sub> = H, C1-3 alkyl, aralkyl; m = 0, 1; n = 0-2] are prepd. which are thrombin catalytic site inhibitors and are useful as anticoagulants. These compds. show selectivity for thrombin over other trypsinlike enzymes and have oral bioavailability. Thus, FeCl<sub>3</sub>-induced thrombotic occlusion of the rat carotid artery was prevented by N-methyl-D-phenylalanyl-L-prolyl-3(S)-(4-aminocyclohexyl)-2-oxo-β-alanine-N-methylamide (II) (10 μg/kg/min i.v.). II inhibited thrombin with K<sub>i</sub> = 0.09 nM, a 12,790-fold selectivity relative to trypsin. II was prepd. in 8 steps from the known 4-benzyloxycarbonylaminocyclohexyl-Nα-(tert-butoxycarbonyl)glycine.

IT 161366-67-2P

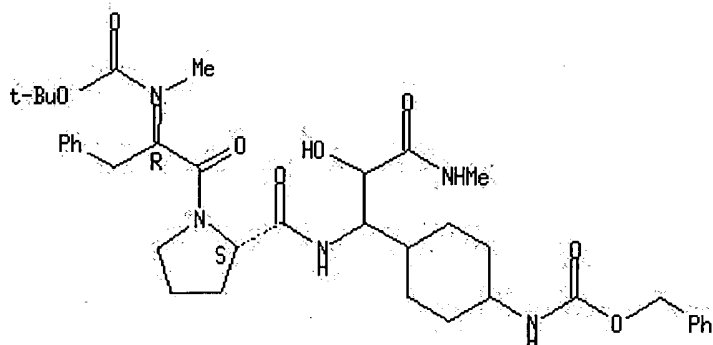
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(thrombin-inhibiting peptide analogs as anticoagulants)

RN 161366-67-2 HCAPLUS

CN β-Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-D-phenylalanyl-L-prolyl-2-hydroxy-N-methyl-3-[4-[(phenylmethoxy)carbonyl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 24 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Citing  
Text References

ACCESSION NUMBER: 1996:71581 HCAPLUS  
DOCUMENT NUMBER: 124:261749  
TITLE: Preparation of peptide antagonists of luteinizing hormone releasing factor.  
INVENTOR(S): Bowers, Cyril Y.; Folkers, Karl A.; Ljungqvist, Anders; Feng, Dong-mei; Janceka, Anna  
PATENT ASSIGNEE(S): Administrators of the Tulane Educational Fund, USA; Board of Regents, the University of Texas System  
SOURCE: U.S., 13 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5480969	A	19960102	US 1992-946056	19920915
US 5656727	A	19970812	US 1995-430602	19950428

PRIORITY APPLN. INFO.: US 1992-946056 A2 19920915

AB LHRH antagonists similar to antide and congeners with higher water soly. have been synthesized by substitutions in positions 1, 5 or 6 with hydrophilic residues. These peptides have antioviulatory activity with minimal histamine releasing effect. Thus, Ac-D-3-Qal-D-pClPhe-D-3-Pal-Ser-cPzACAla-D-PicLys-Leu-Arg-Pro-D-Ala-NH<sub>2</sub> [Argtide, 3-Qal = 3-(3-quinolinyl)alanine, pClPhe = 3-(4-chlorophenyl)alanine, 3-Pal = 3-(3-pyridyl)alanine, cPzACAla = cis-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine, PicLys = Nε-picolinoyllysine], prepd. by solid phase synthesis, showed 89% antioviulatory activity at 0.25 µg in rats.

IT 137584-28-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of peptide antagonists of LHRH)

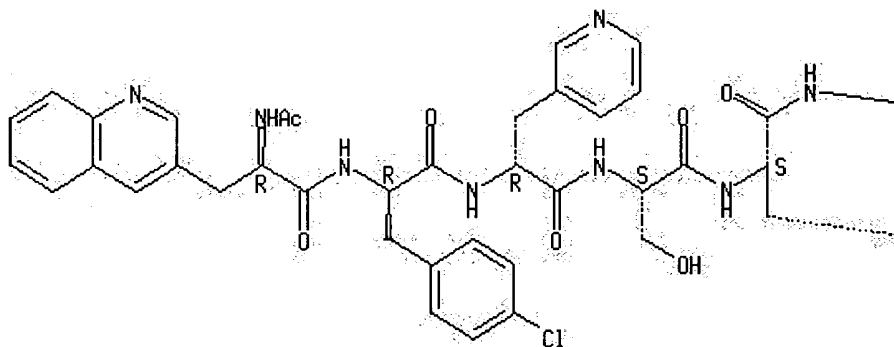
RN 137584-28-2 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(3-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

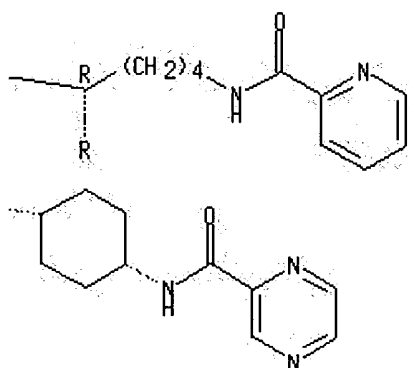
Absolute stereochemistry.



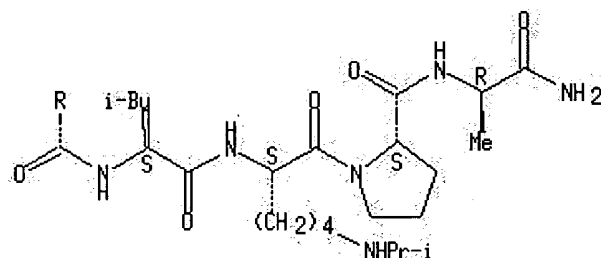
PAGE 1-A



PAGE 1-B



PAGE 2-A



L8 ANSWER 25 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
ACCESSION NUMBER:	1996:13304 HCAPLUS
DOCUMENT NUMBER:	124:203099
TITLE:	Preparation of peptide analog LHRH antagonists with low histamine release.
INVENTOR(S):	Folkers, Karl A.; Ljungqvist, Anders; Feng, Dong Mei; Kubota, Minoru; Tang, Pui Fun L.; Bowers, Cyril Y.
PATENT ASSIGNEE(S):	Board of Regents, University of Texas System, USA; Administrators of the Tulane Educational Fund
SOURCE:	U.S., 20 pp. Cont.-in-part of U.S. 4,935,491.
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2
PATENT INFORMATION:	

ACCESSION NUMBER: 1996:13304 HCAPLUS  
 DOCUMENT NUMBER: 124:203099  
 TITLE: Preparation of peptide analog LHRH antagonists with low histamine release.  
 INVENTOR(S): Folkers, Karl A.; Ljungqvist, Anders; Feng, Dong Mei; Kubota, Minoru; Tang, Pui Fun L.; Bowers, Cyril Y.  
 PATENT ASSIGNEE(S): Board of Regents, University of Texas System, USA; Administrators of the Tulane Educational Fund  
 SOURCE: U.S., 20 pp. Cont.-in-part of U.S. 4,935,491.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5470947	A	19951128	US 1989-371552	19890626
US 4935491	A	19900619	US 1987-88431	19870824
EP 377665	A1	19900718	EP 1988-908786	19880824
EP 377665	B1	19950712		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 59940	A2	19920728	HU 1988-5868	19880824
HU 213098	B	19970228		
US 5763404	A	19980609	US 1995-466333	19950606
PRIORITY APPLN. INFO.:			US 1987-88431	A2 19870824
			US 1989-371552	A3 19890626

OTHER SOURCE(S): MARPAT 124:203099

AB AA1-D-pClPhe-D-3Pal-Ser-AA5-AA6-AA7-AA8-Pro-D-Ala-NH2 [AA1 = Ac-D-2Nal, D-pClPhe, D-Cl2Phe; AA5 = Tyr, NicLys, PicLys, MNicLys, MPicLys, INicLys, DMGLys, PzclLys, c-PzACAla; AA6 = D-NicLys, D-PicLys, D-MNicLys, D-MPicLys, D-INicLys, D-BzLys, D-PzclLys, D-PzACAla, D-NACAla, D-PACAla; AA7 = Leu, Aile, Nle, Val, NVal, Abu, Ala; AA8 = ILys, IOrn; MNicLys = NE -(6-methylnicotinoyl)lysine; MPicLys = NE -(6-methylpicolinoyl)lysine; NACAla = 3(4-nicotinoylaminocyclohexyl)alanine; 2-Nal = 3-(2-naphthyl)alanine; NicLys = NE -nicotinoyllysine; NicOrn = Nd -nicotinoylornithine; Nle = norleucine; NMeLeu = N-methylleucine; Nval = norvaline; PACAla = 3(4-picolinoylaminocyclohexyl)alanine; 3-Pal = 3-(3-pyridyl)alanine; pClPhe = 3-(4-chloro)phenylalanine; PicLys = NE -picolinoyllysine; Pip = piperidine-2-carboxylic acid; PmcLys = NE -(4-pyrimidinylcarbonyl)lysine; PmACAla = 3[4(4-pyrimidinylcarbonyl)aminocyclohexyl]alanine; PzACAla = 3(4-pyrazinylcarbonylaminocyclohexyl)alanine; 3-PzAla = 3-pyrazinylalanine; PzclLys = NE -pyrazinylcarbonyllysine; INicLys = NE -isonicotinoyllysine; DMGLys = NE -(N,N-dimethylglycyl)lysine; Aile = alloseleucine; Abu = 2-aminobutyric acid; ILys = NE -isopropyllysine; IOrn = Nd-isopropylornithine], and other Antide-related peptides, were prepd. Ac-D-2-Nal-D-pClPhe-D-3-Pal-Ser-PicLys-cis-DpZACAla-Leu-ILys-Pro-D-Ala-NH2 was one of the most potent and had higher antioviulatory activity than Antide, i.e. 73%/0.25 µg and 100%/0.5 µg vs. 36%/0.5 µg and 100%/1.0 µg. Antide showed significant (p<0.001) duration of action when injected at 10 ug 44 h before 50 ng of the agonist [D-3-Qal6]-LHRH. Antide showed oral AOA at 600 ug (73%) and at 1200 ug (100%) with negligible difference being found between water and corn oil oral formulations.

IT 174397-27-4P

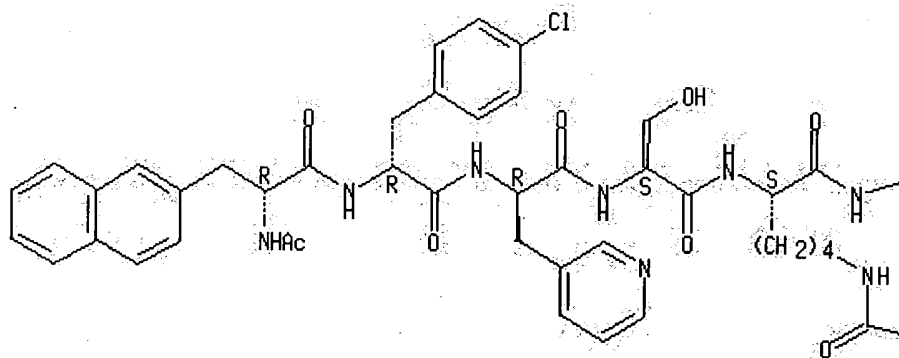
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of peptide analog LHRH antagonists with low histamine release)

RN 174397-27-4 HCAPLUS

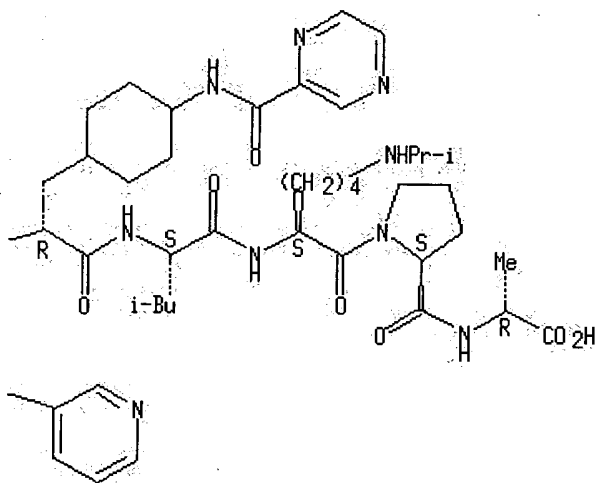
CN D-Alanine, N-[1-[N2-[N-[N-[N2-[N-[N-[N-[N-acetyl-3-(2-naphthalenyl)-D-alanyl]-4-chloro-D-phenylalanyl]-3-(3-pyridinyl)-D-alanyl]-L-seryl]-N6-(3-pyridinylcarbonyl)-L-lysyl]-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-D-alanyl]-L-leucyl]-N6-(1-methylethyl)-L-lysyl]-L-prolyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L8 ANSWER 26 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:471251 HCAPLUS  
 DOCUMENT NUMBER: 122:230975  
 TITLE: Antide B, an antagonist of LHRH with cis-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine in position 5  
 AUTHOR(S): Janecka, A.; Janecki, T.; Bowers, C.; Folkers, K.  
 CORPORATE SOURCE: Inst. Biomedical Res., Univ. Texas Austin, Austin, TX, USA  
 SOURCE: Amino Acids (1995), 8(1), 89-96  
 CODEN: AACIE6; ISSN: 0939-4451  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Several LHRH antagonists with trans-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine (trans-pzACala) in the position 5 were synthesized and their antioovulatory activity was compared with the activity of the analogs contg. cis-PzACala in this position. In all cases cis-isomer produced more potent analogs. Introduction of cis-PzACala in the position 5 of Antide gave Antide B which completely inhibits ovulation at a dose of 0.5

$\mu\text{g/rat}$ . Antide B releases negligible histamine ( $\text{ED}_{50} = 104 \mu\text{g/mL}$ ), and has excellent soly. in water. Also, an improved synthesis of cis-PzACAla is reported, involving the hydrogenation of 4-aminophenylalanine on a rhodium catalyst to give the desired cis-isomer with a 53% yield.

## IT 118427-62-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

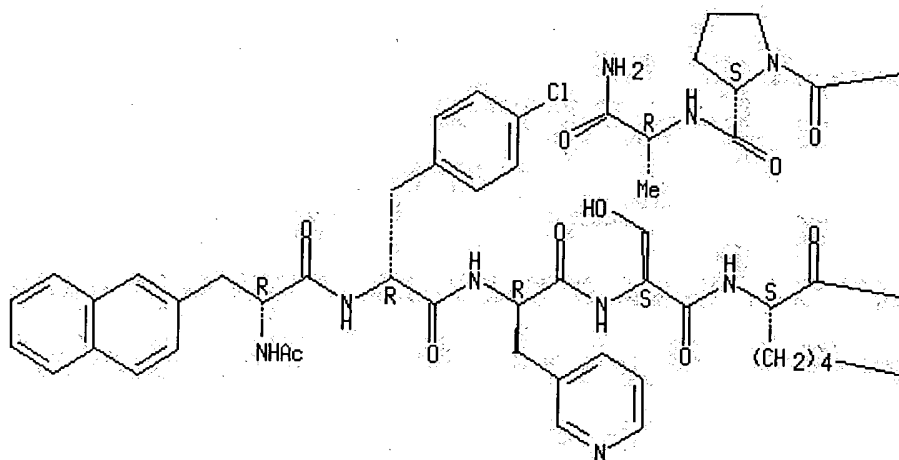
(an antagonist of LHRH with cis-3-(4-pyrazinylcarbonylamino)cyclohexyl)alanine in position 5)

RN 118427-62-6 HCAPLUS

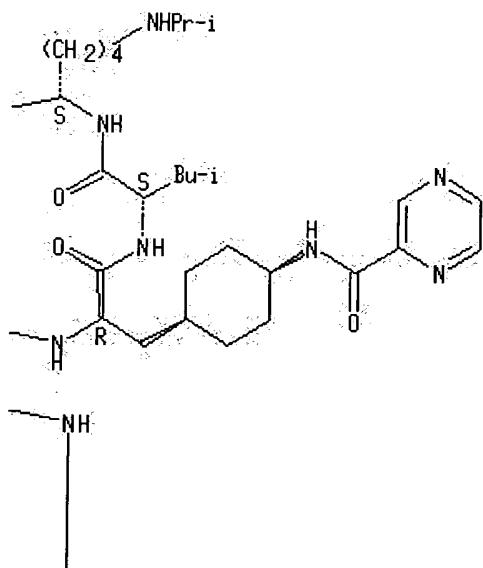
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N6-(2-pyridinylcarbonyl)-L-lysyl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-D-alanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



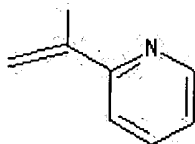
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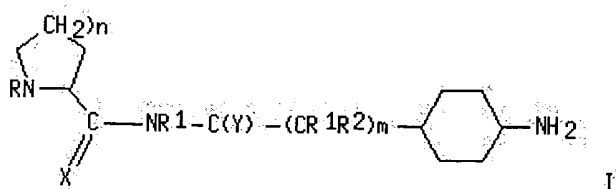


L8 ANSWER 27 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1995:397257 HCAPLUS  
 DOCUMENT NUMBER: 122:178392  
 TITLE: Preparation of cyclohexamine derivatives for thrombin inhibitors  
 INVENTOR(S): Veber, Daniel F.; Lewis, S. Dale; Shafer, Jules A.; Feng, Dong-Mei; Nutt, Ruth F.; Brady, Stephen F.  
 PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
 SOURCE: PCT Int. Appl., 39 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425051	A1	19941110	WO 1994-US4539	19940425
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2159834	AA	19941110	CA 1994-2159834	19940425
AU 9467738	A1	19941121	AU 1994-67738	19940425
AU 670381	B2	19960711		
EP 699074	A1	19960306	EP 1994-915883	19940425
EP 699074	B1	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08509735	T2	19961015	JP 1994-524463	19940425
JP 3486412	B2	20040113		
AT 227581	E	20021115	AT 1994-915883	19940425
ES 2184763	T3	20030416	ES 1994-915883	19940425
PRIORITY APPLN. INFO.:				
			US 1993-55611	A 19930430
			WO 1994-US4539	W 19940425
OTHER SOURCE(S): MARPAT 122:178392				
GI				



AB 4-Substituted cyclohexylamine derivs. are disclosed which are thrombin catalytic site inhibitors and which are useful as anticoagulants. These compds. show selectivity for thrombin over other trypsin-like enzymes and have oral bioavailability. Compds. I and II [ $m = 0, 1$ ;  $n = 0-2$ ;  $X = O, H_2$ ;  $R =$  arylsulfonyl, aminoacyl, acylaminoacyl, etc.;  $R_1, R_2 = H, Me$ ;  $R_3 = H, C1-3$  alkyl, (substituted) aryl, etc.;  $Y = CHO, COCF_3, COOH$ , etc.] are claimed. Prepn. of compds. of the invention is included, as are thrombin inhibitory ( $K_i$ ) data.

IT **161366-67-2P**

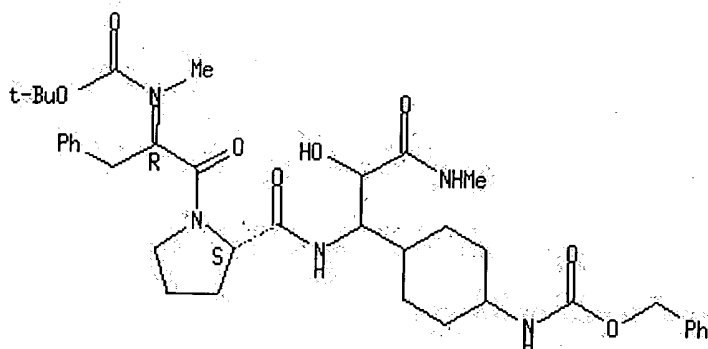
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(cyclohexylamine deriv. prepn. for thrombin inhibition)

RN **161366-67-2** HCAPLUS

CN  $\beta$ -Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-D-phenylalanyl-L-prolyl-2-hydroxy-N-methyl-3-[4-[[ (phenylmethoxy)carbonyl]amino]cyclohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 28 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1995:340197 HCAPLUS
DOCUMENT NUMBER:	122:188158
TITLE:	N5-Pyrazinylcarbonylornithine, an effective substituent for position 5 of antagonists of LHRH
AUTHOR(S):	Janecka, Anna; Koerber, Steven; Janecki, Tomasz; Bowers, Cyril; Folkers, Karl
CORPORATE SOURCE:	Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA
SOURCE:	Zeitschrift fuer Naturforschung, B: Chemical Sciences (1995), 50(1), 147-50 CODEN: ZNBSEN; ISSN: 0932-0776
PUBLISHER:	Verlag der Zeitschrift fuer Naturforschung
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Computer modeling was used to find an effective substituent for position 5 in antagonists of the LH-releasing hormone (LHRH). In particular, it was desired to replace cis-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine (cPzACala) in position 5 because this substituent is laborious to

synthesize. Calcns. revealed that N5-pyrazinylcarbonylornithine (PzOrn) should be a suitable substitute for cPzACala, with N6-pyrazinylcarbonyllysine (PzLys) being a second choice. Twelve analogs were synthesized in four series with 3-(2-naphthyl)-D-alanine (D-Nal) or 3-(3-quinolinyl)-D-alanine (D-Qal) in position 1, and N6-isopropyllysine (ILys) or Arg in position 8. Biol. assays validated the calcns. and show that antagonists with PzOrn were comparable in antioviulatory activity (AOA) with antagonists with cPzACala. What is also important, antagonists with PzOrn released significantly less histamine than those with cPzACala.

IT 137584-28-2DP, Lystide, (pyrazinylcarbonyl)ornithine-contg.

analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

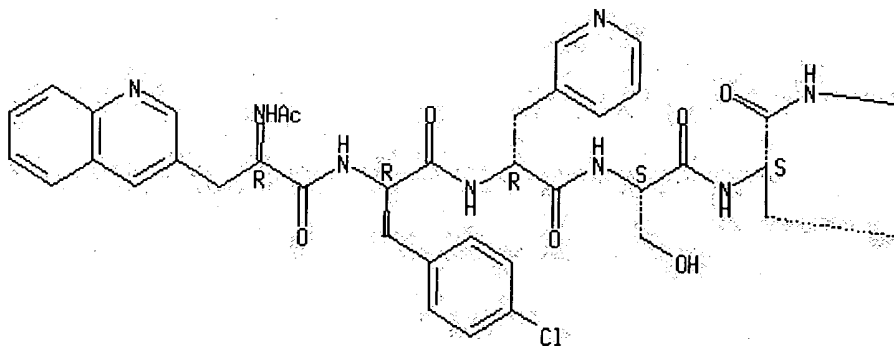
(prepn. and antioviulatory activities of (pyrazinylcarbonyl)ornithine-contg. LH-RH antagonists)

RN 137584-28-2 HCAPLUS

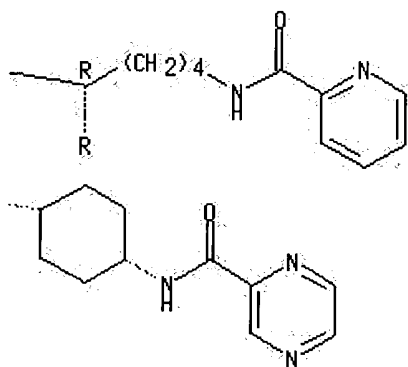
CN D-Alaninamide, N-acetyl-3-(3-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

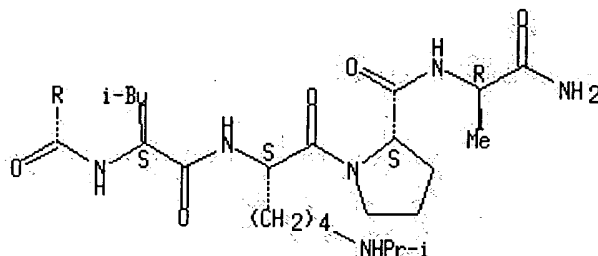
PAGE 1-A



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L8 ANSWER 29 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1994:655277 HCAPLUS  
 DOCUMENT NUMBER: 121:255277  
 TITLE: Synthesis and biological study of bis(2-chloroethyl) sulfides containing carboxylic groups. 3. Cyclohexylamides of 3(or 4)-chloro-4(or 3)-[(2-chloroethyl)thio]butanoic acids  
 AUTHOR(S): Rasteikiene, L.; Vektariene, A.; Pociute, N.; Mikulskiene, G.; Valaviciene, J.  
 CORPORATE SOURCE: Institute Chemistry, Vilnius, Lithuania  
 SOURCE: Chemija (1993), (3), 64-7  
 CODEN: CHMJES; ISSN: 0235-7216  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

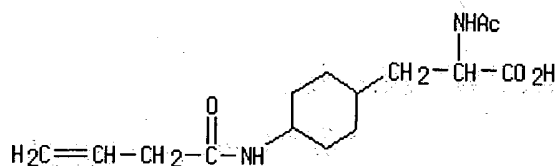
AB Cyclohexylamides Cl(CH<sub>2</sub>)<sub>2</sub>SCH(CH<sub>2</sub>Cl)CH<sub>2</sub>CONHC<sub>6</sub>H<sub>10</sub>R and Cl(CH<sub>2</sub>)<sub>2</sub>SCH<sub>2</sub>CHClCH<sub>2</sub>CONHC<sub>6</sub>H<sub>10</sub>R-4 (C<sub>6</sub>H<sub>10</sub> = cyclohexane moiety, R = H, cis- or trans-CO<sub>2</sub>H, or -CH<sub>2</sub>CO<sub>2</sub>H, cis-β-substituted-DL-Ac-β-Ala-OH) were prepd. by addn. reaction of butenamides with Cl(CH<sub>2</sub>)<sub>2</sub>SCl. The biol. assay shows that the products are less toxic than analogous acids or phenylamides, whereas their antitumor effect remains high.

IT 158609-00-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (synthesis and antitumor activity of cyclohexylamides of chloro[(chloroethyl)thio]butanoic acids)

RN 158609-00-8 HCAPLUS

CN Cyclohexanepropanoic acid, α-(acetylamino)-4-[(1-oxo-3-butenyl)amino]- (9CI) (CA INDEX NAME)



L8 ANSWER 30 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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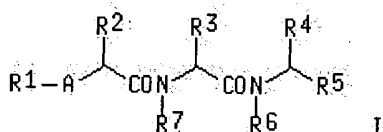
ACCESSION NUMBER: 1994:410003 HCAPLUS  
 DOCUMENT NUMBER: 121:10003  
 TITLE: Preparation of peptides by reaction of olefinic alcohol and enol ether for treatment of tachypnea and myocardial reperfusion injury.  
 INVENTOR(S): Itsumi, Keiji; Kei, Seihaku; Fukami, Jikiki; Hashihon, Sanashi



PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 131 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05208914	A2	19930820	JP 1992-233604	19920901
US 5430022	A	19950704	US 1993-86094	19930706
US 5656604	A	19970812	US 1995-422944	19950417
PRIORITY APPLN. INFO.:			US 1991-753997	19910903
			GB 1990-10740	19900514
			GB 1990-26254	19901203
			GB 1991-4064	19910227
			US 1991-696701	19910507
			US 1992-845056	19920303
			US 1993-86094	19930706

OTHER SOURCE(S): MARPAT 121:10003  
 GI



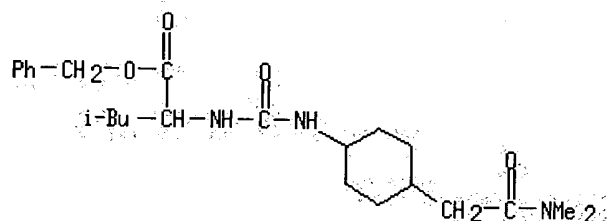
AB Title compds. I [R1 = H, acyl; R2 = alkyl, (un)substituted aralkyl, cycloalkylalkyl, (un)substituted heterocyclalkyl; R3 = (un)substituted heterocyclalkyl, (un)substituted aralkyl; R4 = H, (un)substituted alkyl; R5 = carboxy, (un)protected carboxy, (un)protected carboxyalkyl; R6 = H, (un)substituted alkyl; R7 = H, alkyl; A = O, NH, alkylimino, alkylene; with provisos], useful for the treatment of many cardiovascular injury, e.g., hypertension, are prepd. Thus, a mixt. of N-phenylacetyl-Leu-OH and H-D-Trp(Me)-D-Phe-OMe.HCl in DMF was stirred with ice cooling for 4.5 h to give PhCH2CO-Leu-D-Trp(Me)-D-Phe-OMe. In an in vitro study, Q-Leu-D-Trp(Me)-D-Pya-OH.HCl [Q = cyclohexylcarbonyl, Pya = 2-pyridylalanine] (also prepd.) had an IC50 of 2.3x10<sup>-9</sup> M against the binding of 125-I-endothelin-1 with pig aorta receptors.

IT. 142380-82-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as intermediate for peptides for treatment of tachypnea and myocardial reperfusion injury)

RN 142380-82-3 HCAPLUS

CN L-Leucine, N-[[[4-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]amino]carbonyl]-, phenylmethyl ester, cis- (9CI) (CA INDEX NAME)



L8 ANSWER 31 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1994:236341 HCAPLUS  
 DOCUMENT NUMBER: 120:236341  
 TITLE: Effective antagonists of luteinizing hormone releasing hormone modified at position one  
 AUTHOR(S): Janecka, A.; Janecki, T.; Bowers, C.; Folkers, K.  
 CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, USA  
 SOURCE: Amino Acids (1993), 5(3), 359-65  
 CODEN: AACIE6; ISSN: 0939-4451  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The amino acid, D-2-naphthylalanine, has been used by many investigators as a substituent for position one of antagonists of LH-RH. The authors have newly designed substituents for position one in which the carboxy groups of 2-naphthoic acid, 3-quinoline- and 2-quinoxaline-carboxylic acids are linked to the five amino acids, D-Ala, D-Thr, D-NVal, D-Ser, and Gly. The substituents in positions 2-10 were D-pClPhe<sup>2</sup>, D-Pal<sup>3</sup>, Ser<sup>4</sup>, PicLys<sup>5</sup>, D-PicLys<sup>6</sup>, Leu<sup>7</sup>, ILys<sup>8</sup>, Pro<sup>9</sup>, D-Ala-NH<sup>210</sup>. Remarkably, D-Thr, acylated on the amino group by 3-quinolinecarboxylic acid or by 3-quinoxalinecarboxylic acid, and introduced into position one of a relatively potent antagonist, gave a new class of antagonists of LHRH, which released as little histamine as yet recorded, and yet possessed reasonable anti-ovulatory activity and greatly improved soly. These structure-activity results advance the basic knowledge of understanding the structural features of such decapeptides which cause antioviulatory activity and histamine release.

IT 154427-73-3

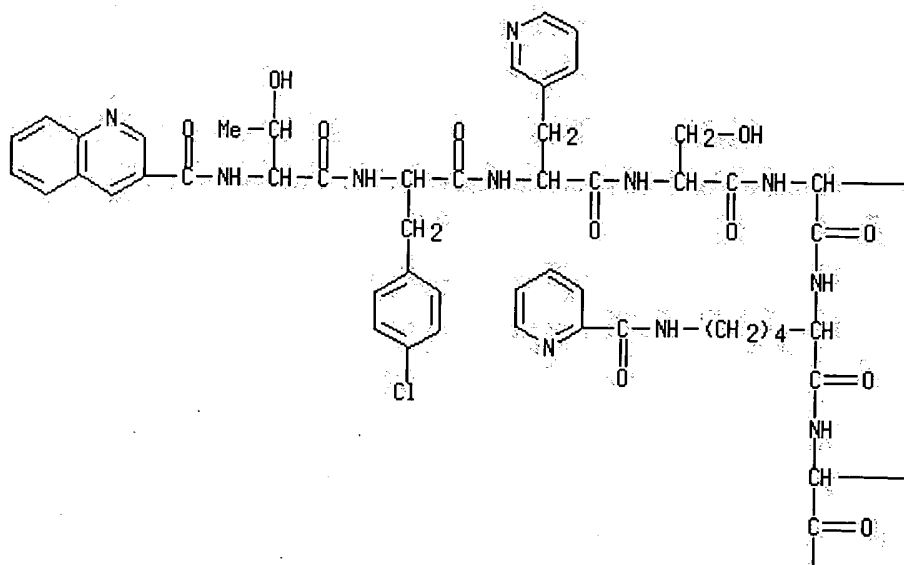
RL: BIOL (Biological study)

(histamine-releasing and ovulation-inhibiting activity of, structure in relation to)

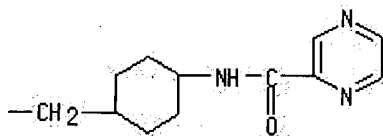
RN 154427-73-3 HCAPLUS

CN D-Alaninamide, N-(3-quinolinylcarbonyl)-D-threonyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-L-arginyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

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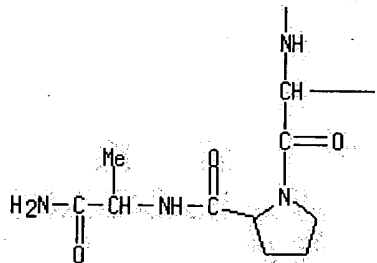


PAGE 1-B

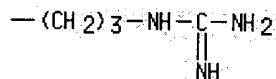


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PAGE 2-A



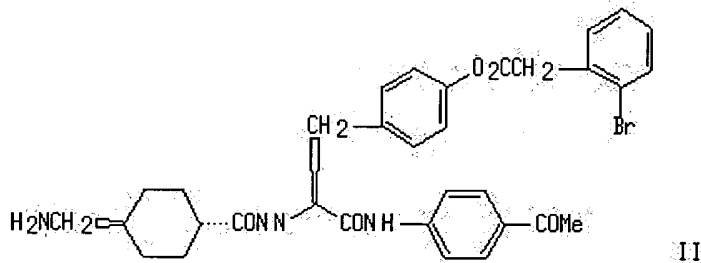
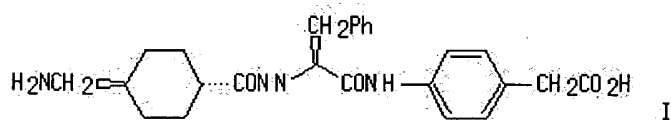
PAGE 2-B



L8 ANSWER 32 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1994:135102 HCAPLUS
DOCUMENT NUMBER:	120:135102
TITLE:	Development of active center-directed plasmin and plasma kallikrein inhibitors and studies on the structure-inhibitory activity relationship
AUTHOR(S):	Teno, Naoki; Wanaka, Keiko; Okada, Yoshio; Taguchi, Hiroaki; Okamoto, Utako; Hijikata-Okunomiya, Akiko; Okamoto, Shosuke
CORPORATE SOURCE:	Fac. Pharm. Sci., Kobe-Gekuin Univ., Kobe, 651-21, Japan
SOURCE:	Chemical & Pharmaceutical Bulletin (1993), 41(6), 1079-80 CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE:	Journal
LANGUAGE:	English
GI	



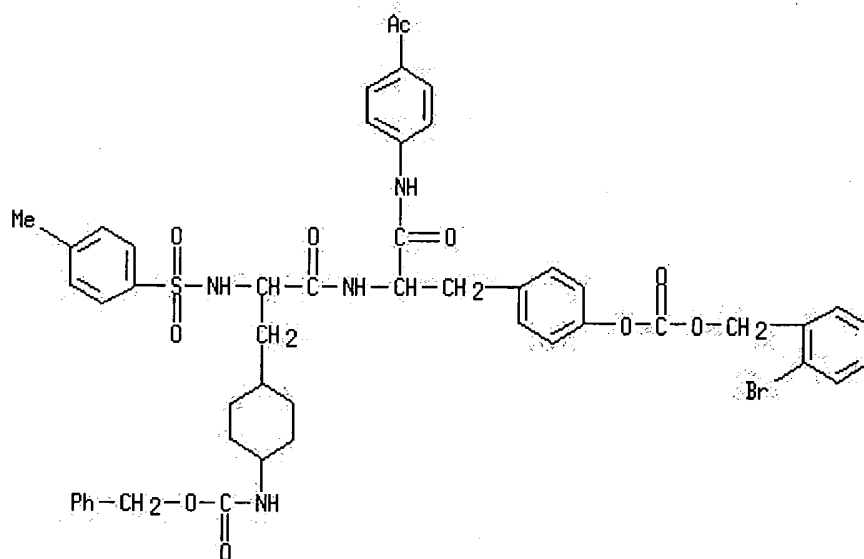
AB Phenylalanine anilide I, a potent and selective inhibitor of plasma kallikrein, can be divided into three parts (P1, P1' and P2'), each of which contains one of the rings. Each part was substituted with various other moieties in order to study the relationship between the structure and inhibitory activities toward plasmin, plasma kallikrein, urokinase and thrombin. Tyrosine anilide II inhibited plasma and plasma kallikrein with IC<sub>50</sub> values of  $2.3 \times 10^{-7}$  M and  $3.7 \times 10^{-7}$  M, and K<sub>i</sub> values of  $1.2 \times 10^{-7}$  M and  $1.3 \times 10^{-7}$  M, resp.

IT **152438-56-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and acidic deblocking of)

RN **152438-56-7** HCAPLUS

CN L-Tyrosinamide, N-[(4-methylphenyl)sulfonyl]-3-[4-  
[[ (phenylmethoxy) carbonyl] amino] cyclohexyl]-L-alanyl-N-(4-acetylphenyl)-,  
(2-bromophenyl)methyl carbonate (ester), trans- (9CI) (CA INDEX NAME)



L8 ANSWER 33 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1994:54935 HCAPLUS

DOCUMENT NUMBER: 120:54935

TITLE: Synthesis and bioassay of LH-RH-antagonists with  
N-Ac-D-O-phenyltyrosine and N-Ac-D-3-(2-  
dibenzofuranyl)alanine in position 1

AUTHOR(S): Ljungqvist, Anders; Bowers, Cyril Y.; Folkers, Karl

CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, USA

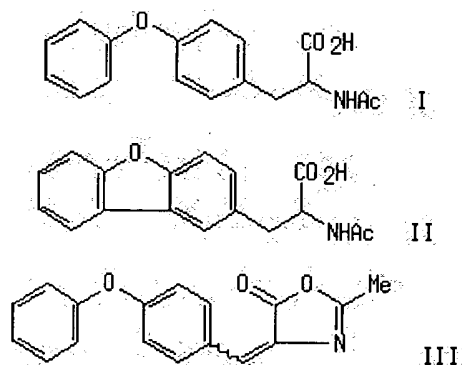
SOURCE: International Journal of Peptide & Protein Research  
(1993), 41(5), 427-32  
CODEN: IJPPC3; ISSN: 0367-8377

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 120:54935

GI



AB N-acetyl-D-O-phenyltyrosine (D-I) and N-acetyl-D-3-(2-dibenzofuranyl)alanine (D-II) were prepd. from azlactone III. Resoln. of the Me ester of DL-I by subtilisin Carlsberg gave L-I and the Me ester of D-I. The Me ester of D-I was sapond. to give D-I. Treatment with palladium(II) acetate in trifluoroacetic acid converted D-I into D-II. D-I and D-II were incorporated instead of N-Ac-D-2-Nal into position 1 of the LH-releasing hormone (LHRH) antagonist (N-Ac-D-2-Nal1,D-pClPhe2,D-3-Pal3,c-PzACAla5,D-PicLys6,Ilys8,D-Ala10)-LHRH [2-Nal = 3-(2-naphthyl)alanine, 3-Pal = 3-(3-pyridyl)alanine, c-PzACAla = cis-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine, PicLys = N $\epsilon$ -picolinyllysine, Ilys = N $\epsilon$ -isopropyllysine]. The more rigid D-II was structurally more effective than D-I; the AOA's for the corresponding analogs were 82 and 38%, resp., at 0.5  $\mu$ g. Replacement of c-PzACAla in position 5 by O-phenyltyrosine significantly decreased potency.

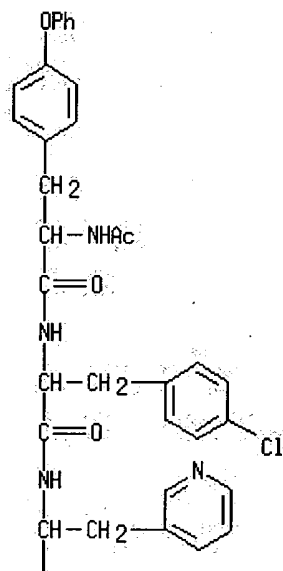
IT **150351-70-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and LH-releasing hormone antagonistic activity of)

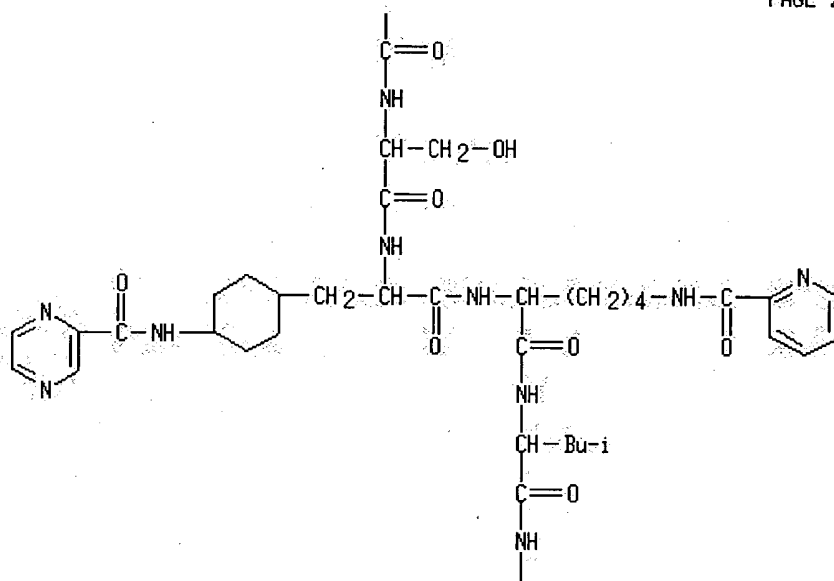
RN **150351-70-5** HCAPLUS

CN D-Alaninamide, N-acetyl-O-phenyl-D-tyrosyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N $\epsilon$ -(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N $\epsilon$ -(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

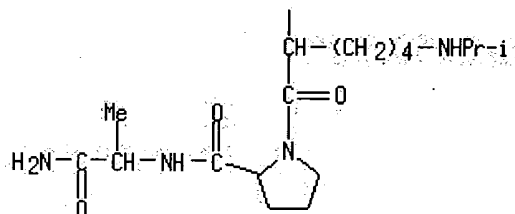
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L8 ANSWER 34 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1993:671686 HCAPLUS  
 DOCUMENT NUMBER: 119:271686  
 TITLE: Antagonists of LHRH with histidine in the priority position 8  
 AUTHOR(S): Janecka, Anna; Shan, Si Mei; Bowers, Cyril; Folkers, Karl  
 CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, USA  
 SOURCE: Zeitschrift fuer Naturforschung, B: Chemical Sciences (1993), 48(6), 812-16  
 CODEN: ZNBSEN; ISSN: 0932-0776  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

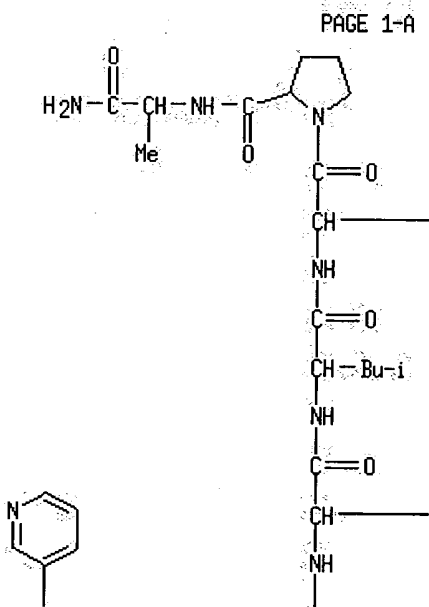
AB Sixteen new designs of antagonists of the LH releasing hormone (LHRH) with histidine in position 8 were synthesized, because this position is crit. both for antioviulatory activity and the side effect of histamine release. The most potent antagonist was Ac-D-Qal-D-p-ClPhe-D-3-Pal-Ser-cPzACAla-D-Lys(Pic)-Leu-His-Pro-D-Ala-NH<sub>2</sub> [Qal = 3-(3-quinolyl)alanine, p-ClPhe = p-chlorophenylalanine, 3-Pal = 3-(3-pyridylalanine), cPzACAla = cis-3-(4-pyrazinylcarbonylaminocyclohexyl)alanine, Pic = picolinoyl], which showed 33% antioviulatory activity at 0.25 µg. The histamine release was remarkably negligible at an ED<sub>50</sub> of 308 µg/mL, which is superior to 186 µg/mL for LHRH and comparable to 300 for Antide. The relative basicities of His, Arg, and Lys(CHMe<sub>2</sub>) in position 8 of the antagonists influences both the level of antioviulatory potency and a negligible to a significant release of histamine. The least basic His<sub>8</sub> analogs can have the lowest antioviulatory activity and the highest ED<sub>50</sub>. The very basic Arg<sub>8</sub> analogs can have the highest antioviulatory activity and the lowest ED<sub>50</sub>. The moderately basic Lys(CHMe<sub>2</sub>)<sub>8</sub> analogs can be a compromise for acceptable levels of potency and safety.

IT 151546-16-6P

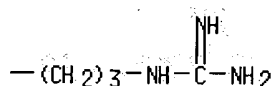
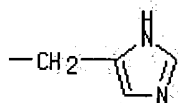
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, by solid-phase methods and antioviulatory activity of)

RN 151546-16-6 HCAPLUS

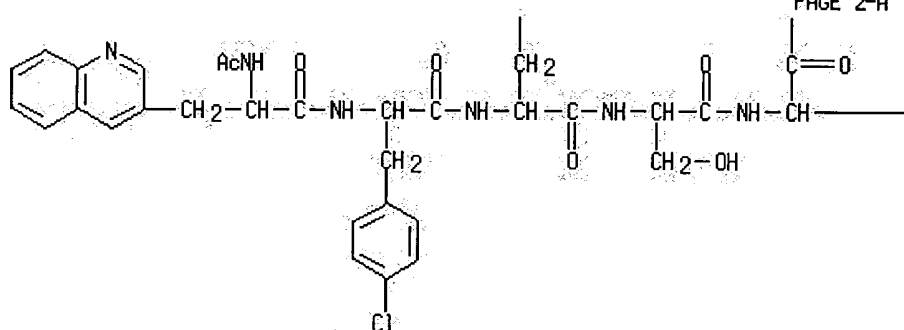
CN D-Alaninamide, N-acetyl-3-(3-quinolyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-D-arginyl-L-leucyl-L-histidyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)



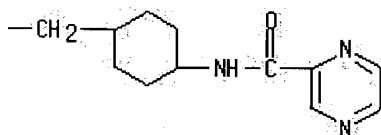
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L8 ANSWER 35 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1993:440171 HCAPLUS  
 DOCUMENT NUMBER: 119:40171  
 TITLE: Hepatocellular uptake of peptides. II. Interactions between hydrophilic linear renin-inhibiting peptides and transport systems for endogenous substrates in liver cells  
 AUTHOR(S): Seeberger, Agnes; Ziegler, Kornelia  
 CORPORATE SOURCE: Inst. Pharmakol. Toxikol., Justus-Liebig Univ., Giessen, 6300, Germany  
 SOURCE: Biochemical Pharmacology (1993), 45(4), 917-25  
 CODEN: BCPA6; ISSN: 0006-2952  
 DOCUMENT TYPE: Journal



LANGUAGE: English

AB To define the endogenous transport system responsible for the hepatocellular uptake of hydrophilic linear peptides, interactions between the cationic renin inhibitor peptide EMD-56133 and substrates of endogenous transport systems of liver cells were studied in isolated rat liver hepatocytes. EMD-56133 competitively inhibited the uptake of ouabain ( $K_i = 75 \mu\text{M}$ ) and vice versa ( $K_i = 200 \mu\text{M}$ ). The sodium-dependent and sodium-independent uptake of cholate and the total uptake of taurocholate were non-competitively blocked by EMD-56133, whereas EMD-56133 did not interfere with the transport systems for monovalent org. cations, amino acids, and long chain fatty acids. The uptake of rifampicin was increased in the presence of EMD-56133. The transport of EMD-56133 was noncompetitively inhibited by cholate ( $K_i = 126 \mu\text{M}$ ) and taurocholate ( $K_i = 44 \mu\text{M}$ ), and uncompetitively inhibited by the linear peptide EMD-51921. The uncharged compd. ouabain ( $K_i = 200 \mu\text{M}$ ) and the bivalent org. cation d-tubocurarine ( $K_i = 370 \mu\text{M}$ ) competitively inhibited the uptake of EMD-56133. Several substrates of other endogenous transport systems (bilirubin, cyclopeptides, monovalent cations, dipeptides, amino acids, fatty acids, hexoses) did not interfere with the transport of EMD-56133. Thus, transport systems for bivalent org. cations or uncharged compds. (ouabain) are able to eliminate EMD-56133.

IT 148563-07-9

RL: BIOL (Biological study)

(liver hepatocyte uptake of, transport substrates interactions with)

RN 148563-07-9 HCAPLUS

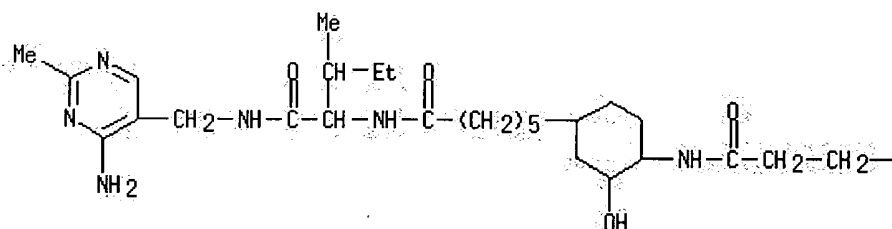
CN  $\beta$ -Alaninamide, N-[4-[(4-amino-1-piperidinyl)carbonyl]phenyl-2,6-t2]-L-alanyl-N-[4-[6-[1-[[[(4-amino-2-methyl-5-pyrimidinyl)methyl]amino]carbonyl]-2-methylbutyl]amino]-6-oxohexyl]-2-hydroxycyclohexyl]-, 2-hydroxy-1,2,3-propanetricarboxylate (salt) (9CI) (CA INDEX NAME)

CM 1

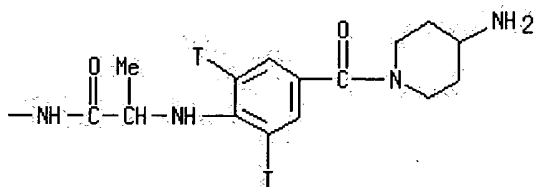
CRN 148563-06-8

CMF C42 H64 N10 O6 T2

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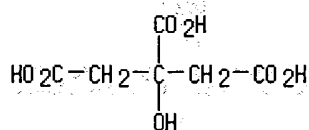


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CM 2

CRN 77-92-9  
CMF C6 H8 O7



L8 ANSWER 36 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1992:543703 HCAPLUS  
DOCUMENT NUMBER: 117:143703  
TITLE: Design, synthesis and bioassays of analogs of Argtide by criteria of potency and safety  
AUTHOR(S): Janecka, Anna; Ljungqvist, Anders; Xu, Jie Cheng; Bowers, Cyril Y.; Folkers, Karl  
CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA  
SOURCE: Medicinal Chemistry Research (1991), 1(5), 306-11  
CODEN: MCREEB; ISSN: 1054-2523  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Thirteen analogs of the LH-RH antagonist, named Argtide, N-Ac-D-3-Qal, D-pClPhe, D-3-Pal, Ser, c-PzACala, D-PicLys, Leu, Arg, Pro, D-AlaNH<sub>2</sub>, with single changes in its sequence have been synthesized toward an increase in potency and/or decrease in histamine release. The most potent of the new analogs is [D-Ptf2]-Argtide which showed 20% anti-ovulatory activity (AOA) at 0.125 µg and 100% at 0.25 µg, and which is superior to Antide. The most safe analog in terms of histamine release was [Cit5]-Argtide which showed an ED<sub>50</sub> 94 µg/mL. D-3-Qal was frequently superior to D-2-Nal in position 1.

IT 138111-66-7D, Argtide, analogs

RL: BIOL (Biological study)

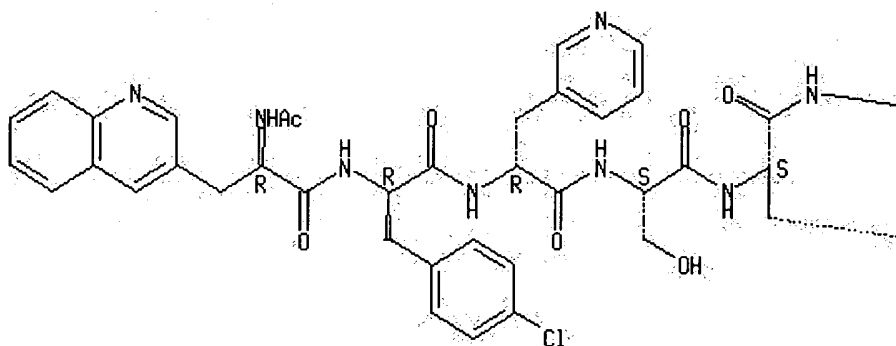
(as LH-RH antagonist, antioviulatory and histamine-releasing activity of, structure in relation to)

RN 138111-66-7 HCAPLUS

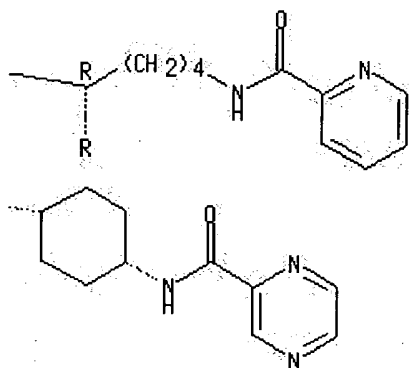
CN D-Alaninamide, N-acetyl-3-(3-quinolinyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[cis-4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-L-arginyl-L-prolyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

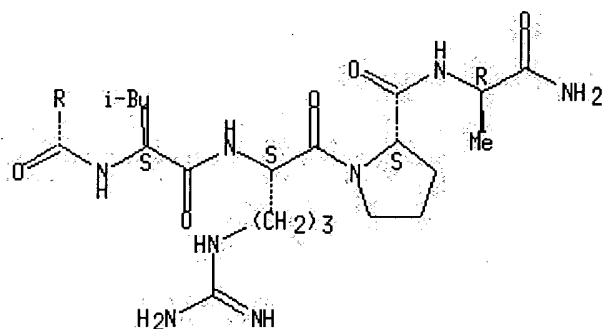
PAGE 1-A



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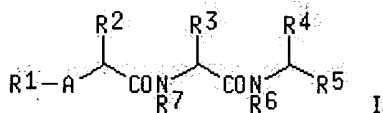
L8 ANSWER 37 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
ACCESSION NUMBER:	1992:449261 HCAPLUS
DOCUMENT NUMBER:	117:49261
TITLE:	Preparation of peptides having endothelin antagonist activity and pharmaceutical compositions comprising them.
INVENTOR(S):	Hemmi, Keiji; Neya, Masahiro; Fukami, Naoki; Hashimoto, Masashi; Tanaka, Hirokazu; Kayakiri, Natsuko
PATENT ASSIGNEE(S):	Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE:	Eur. Pat. Appl., 179 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 457195	A2	19911121	EP 1991-107554	19910509
EP 457195	A3	19921119		
EP 457195	B1	19980415		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9103417	A	19920226	ZA 1991-3417	19910506
US 5284828	A	19940208	US 1991-696701	19910507
AU 9176446	A1	19911114	AU 1991-76446	19910509
AU 644648	B2	19931216		

AT 165100	E	19980515	AT 1991-107554	19910509
NO 9101854	A	19911115	NO 1991-1854	19910513
FI 9102328	A	19911115	FI 1991-2328	19910513
CA 2042442	AA	19911115	CA 1991-2042442	19910513
CN 1057269	A	19911225	CN 1991-103919	19910513
RU 2092491	C1	19971010	RU 1991-4895608	19910513
HU 57233	A2	19911128	HU 1991-1619	19910514
JP 04244097	A2	19920901	JP 1991-206614	19910514
US 5430022	A	19950704	US 1993-86094	19930706
US 5656604	A	19970812	US 1995-422944	19950417
PRIORITY APPLN. INFO.:			GB 1990-10740	19900514
			GB 1990-26254	19901203
			GB 1991-4064	19910227
			US 1991-696701	19910507
			US 1991-753997	19910903
			US 1992-845056	19920303
			US 1993-86094	19930706

OTHER SOURCE(S): MARPAT 117:49261  
GI



AB The title compds. [I; R1 = H, acyl; R2 = alkyl, aralkyl; R3 = (substituted) heterocyclalkyl, (substituted) aralkyl; R4, R6 = H, (substituted) alkyl; R5 = (protected) carboxy, (protected) carboxyalkyl; R7 = H, alkyl; A = O, NH, alkylimino, alkylene; with provisos] were prepd. A mixt. of Q-Leu-OH [Q = PhCH<sub>2</sub>CO], H-D-Trp(Me)-D-Phe-OMe.HCl, and HOBT in DMF was treated with WSCD under ice-bath cooling for 4.5 h, the mixt. was concd. and a soln. of the residue in EtOAc was successively washed with 0.5 N HCl, satd. aq. NaHCO<sub>3</sub>, and brine to give Q-Leu-D-Trp(Me)-D-Phe-OMe. In an assay using porcine aorta tissue Q1-L-Leu-D-Trp(Me)-D-Pya-OEt [Q1 = cyclohexylcarbonyl, Pya = 3-(2-pyridyl)alanine residue; prepn. given] had an IC<sub>50</sub> of 2.3×10<sup>-9</sup> M against 125I-endothelin.

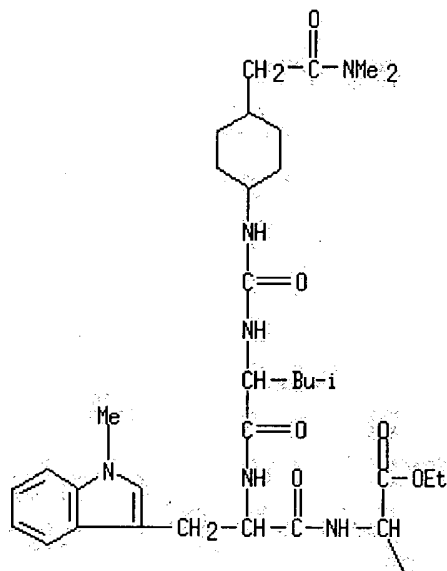
IT 142377-24-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of, as endothelin antagonist)

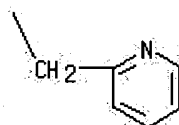
RN 142377-24-0 HCAPLUS

CN D-Alanine, N-[N-[N-[[[4-[2-(dimethylamino)-2-oxoethyl]cyclohexyl]amino]carbonyl]-L-leucyl]-1-methyl-D-tryptophyl]-3-(2-pyridinyl)-, ethyl ester, cis- (9CI) (CA INDEX NAME)

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L8 ANSWER 38 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1992:121867 HCAPLUS  
 DOCUMENT NUMBER: 116:121867  
 TITLE: Linear analogs of atrial natriuretic peptides  
 INVENTOR(S): Scarborough, Robert M.; Lewicki, John A.; Johnson, Lorin K.  
 PATENT ASSIGNEE(S): California Biotechnology, Inc., USA  
 SOURCE: U.S., 62 pp. Cont.-in-part of U.S. Ser. No. 237,299, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5047397	A	19910910	US 1988-285916	19881216
US 4757048	A	19880712	US 1986-868312	19860528
JP 2000191688	A2	20000711	JP 1999-375827	19861103
JP 2002167396	A2	20020611	JP 2001-352364	19861103
ZA 8608434	A	19870930	ZA 1986-8434	19861105
US 4804650	A	19890214	US 1988-168661	19880316
EP 323740	A2	19890712	EP 1988-312221	19881222
EP 323740	A3	19901212		

R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE  
 AU 8929278 A1 19890719 AU 1989-29278 19881222

<u>ZA 8809598</u>	A	19891025	<u>ZA 1988-9598</u>	19881222
<u>JP 03503048</u>	T2	19910711	<u>JP 1989-501372</u>	19881222
<u>JP 2855143</u>	B2	19990210	<u>JP 1988-501372</u>	19881222
<u>IL 88776</u>	A1	19930708	<u>IL 1988-88776</u>	19881223
<u>CA 1340007</u>	A1	19980818	<u>CA 1988-587046</u>	19881223
<u>KR 9709887</u>	B1	19970619	<u>KR 1989-71598</u>	19890824

## PRIORITY APPLN. INFO.:

<u>US 1985-795220</u>	B2	19851105
<u>US 1986-868312</u>	A2	19860528
<u>US 1986-904091</u>	B2	19860904
<u>US 1986-921360</u>	B2	19861028
<u>US 1987-138893</u>	B2	19871224
<u>US 1988-168661</u>	A2	19880316
<u>US 1988-237299</u>	B2	19880826
<u>JP 1986-506065</u>	A3	19861103
<u>JP 1999-375827</u>	A3	19861103
<u>US 1988-285916</u>	A	19881216
<u>WO 1988-US4638</u>	A	19881222

OTHER SOURCE(S): MARPAT 116:121867

AB Compds. (Markush sequences included) and compns. comprising synthetic analogs of atrial natriuretic peptides (ANPs) are provided, along with methods for their prodn. and use as natriuretics, diuretics, and/or vasodilators, or as intermediates for or modulators of such useful compds. or of native ANPs. The invention includes >400 ANP analogs. Prepn., receptor binding activity, and natriuresis and diuresis studies are included for selected analogs.

IT 124833-20-1

RL: PRP (Properties)

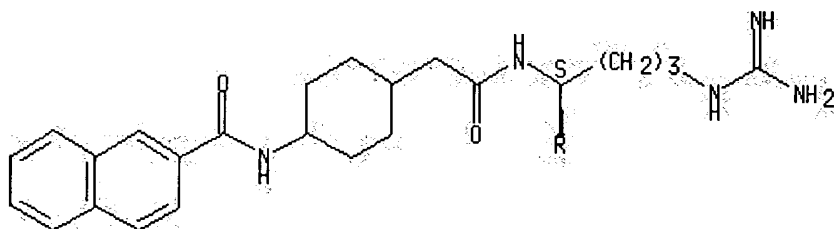
(amino acid sequence of, diuretic and/or natriuretic and/or vasodilator activity in relation to)

RN 124833-20-1 HCAPLUS

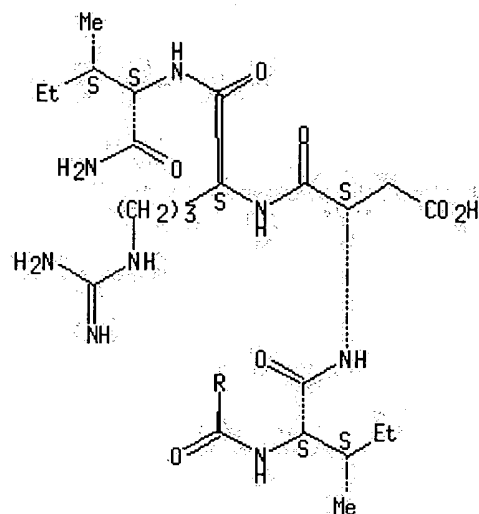
CN L-Isoleucinamide, N2-[[4-[(2-naphthalenylcarbonyl)amino]cyclohexyl]acetyl]-L-arginyl-L-isoleucyl-L- $\alpha$ -aspartyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L8 ANSWER 39 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1992:34706 HCAPLUS  
 DOCUMENT NUMBER: 116:34706  
 TITLE: Superiority of an antagonist of the luteinizing hormone releasing hormone with emphasis on arginine in position 8, named Argtide  
 AUTHOR(S): Janecka, Anna; Ljungqvist, Anders; Bowers, Cyril; Folkers, Karl  
 CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA  
 SOURCE: Biochemical and Biophysical Research Communications (1991), 180(1), 374-9  
 CODEN: BBRCA9; ISSN: 0006-291X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB In the search for more potent antagonists of LH-RH, new peptides with emphasis on arginine in position 8 were designed, synthesized, and tested for anti-ovulatory activity (AOA). Two very potent analogs were achieved. N-Ac-D-3-Qal, D-pClPhe, D-3-Pal, Ser, c-PzACAla, D-PicLys, Leu, Arg, Pro, D-AlaNH<sub>2</sub> showed 63% AOA at 0.125 µg and 89% at 0.25 µg, and an ED<sub>50</sub> of 30.8 µg/mL and may be the most promising antagonist reported. It is named Argtide. N-Ac-D-3-Qal, D-pClPhe, D-3-Pal, Ser, c-PzACAla, D-PicLys, Val, Arg, Pro, D-AlaNH<sub>2</sub> showed 18% AOA at 0.125 µg. Arginine in position 8 of these antagonists may be significant for receptor binding.

IT 118427-65-9

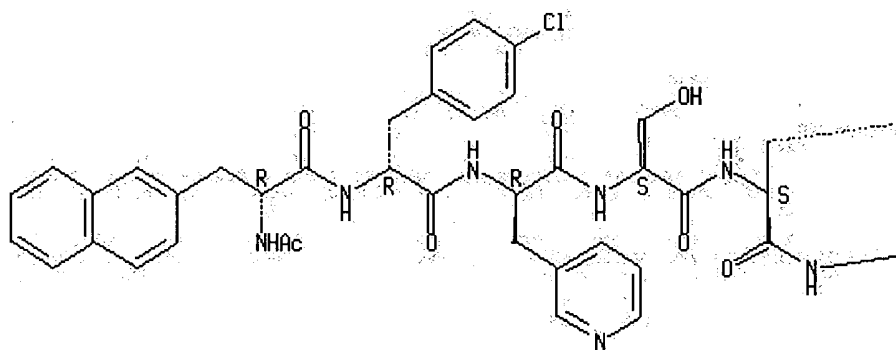
RL: BIOL (Biological study)  
 (LH-RH antagonism by, structure in relation to)

RN 118427-65-9 HCAPLUS

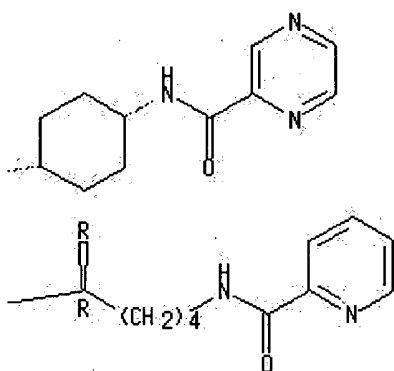
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

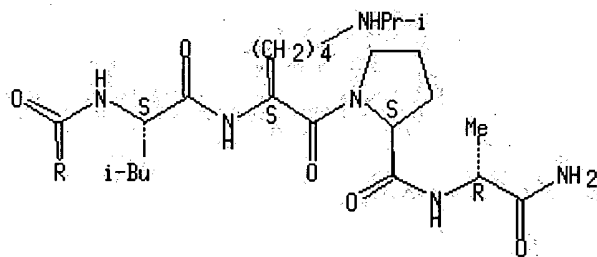
PAGE 1-A



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L8 ANSWER 40 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:

1991:680536 HCAPLUS

DOCUMENT NUMBER:

115:280536

TITLE:

Design, synthesis and biological evaluation of antagonists of LHRH by criteria of potency, safety and solubility

AUTHOR(S):

Ljungqvist, Anders; Feng, Dong Mei; Bowers, Cyril; Hook, William A.; Folkers, Karl

CORPORATE SOURCE:

Inst. Biomed. Res., Univ. Texas, Austin, TX, USA

SOURCE:

Zeitschrift fuer Naturforschung, B: Chemical Sciences (1991), 46(9), 1231-6

CODEN: ZNBSEN; ISSN: 0932-0776

DOCUMENT TYPE:

Journal

LANGUAGE:

English



AB Some analogs of Antide and congeners with higher water soly. have been synthesized by substitutions in positions 1, 5, or 6 with hydrophilic residues. In position 1, D-3-(3-quinolyl)alanine has been incorporated in four peptides and D-3-(3-pyridyl)alanine (Pal) in one peptide. In positions 5 and 6, D- and L-Pal, 3-pyrazolinylalanine, and Lys(H-D-Ser) have been tried. In one peptide, D-Lys(Ac-D-Ser) was substituted in position 6. Most of the new analogs had lower antiovolatory activity than the parent compds., but three potent analogs were identified.

IT 137584-28-2P

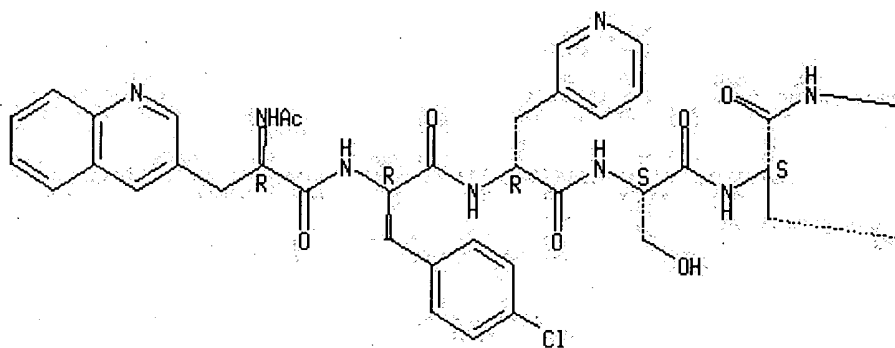
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(prepn. and antiovolatory activity of, histamine release in relation to)

RN 137584-28-2 HCAPLUS

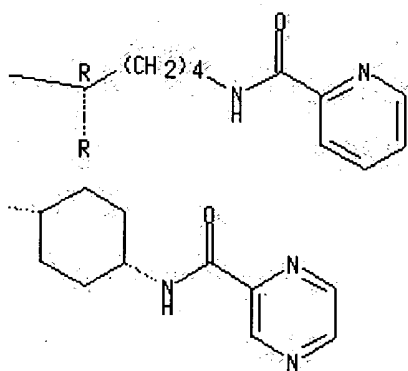
CN D-Alaninamide, N-acetyl-3-(3-quinolyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-L-alanyl-N6-(2-pyridinylcarbonyl)-D-lysyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

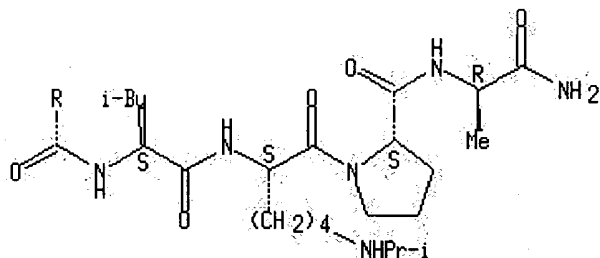
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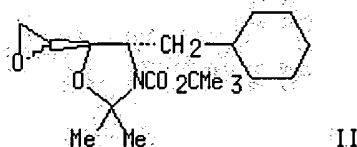
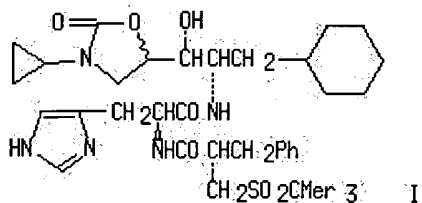
PAGE 2-A



L8 ANSWER 41 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1991:472226 HCAPLUS  
 DOCUMENT NUMBER: 115:72226  
 TITLE: Amino acid derivatives  
 INVENTOR(S): Branca, Quirico; Neidhart, Werner; Ramuz, Henri;  
 Stadler, Heinz; Wostl, Wolfgang  
 PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 71 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 416373	A2	19910313	EP 1990-116088	19900822
EP 416373	A3	19920527		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2023099	AA	19910305	CA 1990-2023099	19900810
AU 9061360	A1	19910307	AU 1990-61360	19900827
AU 646640	B2	19940303		
ZA 9006856	A	19910626	ZA 1990-6856	19900828
HU 58060	A2	19920128	HU 1990-5676	19900829
JP 03099047	A2	19910424	JP 1990-228473	19900831
NO 9003832	A	19910305	NO 1990-3832	19900903
US 5688946	A	19971118	US 1994-277111	19940719
PRIORITY APPLN. INFO.:			CH 1989-3192	19890904
			CH 1990-2336	19900712
			US 1990-571689	19900823

OTHER SOURCE(S): MARPAT 115:72226  
 GI



AB Amino acid derivs. RCONR1CH(CH2R2)CONHCHR3CHR4CR5R6R7 (R-R7 = substituents) were prepd. for use as antihypertensives and renin inhibitors. Thus, amide I was prepd. from epoxide II, H-His-OMe.2HCl, and (S)-PhCH2CH(CO2H)CH2SO2CMe3 in 5 steps. I had a renin-inhibiting ED50 of 0.0009 .mu.M/L.

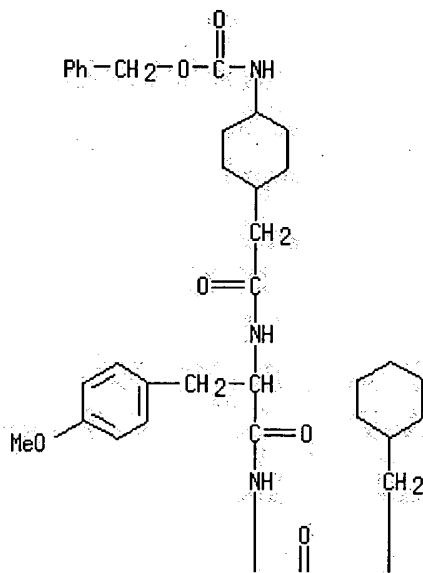
IT 134363-67-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(prepn. and detritylation of)

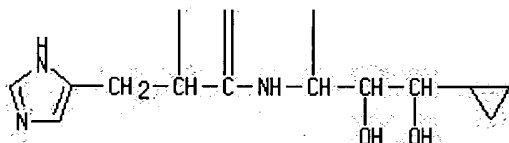
RN 134363-67-0 HCAPLUS

CN L-Histidinamide, O-methyl-N-[[4-[[[(phenylmethoxy) carbonyl]amino]cyclohexyl]  
[acetyl]-L-tyrosyl-N-[1-(cyclohexylmethyl)-3-cyclopropyl-2,3-  
dihydroxypropyl]-, [1(cis),2[1S-(1R\*,2S\*,3R\*)]]- (9CI) (CA INDEX NAME)

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L8 ANSWER 42 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1991:82502 HCAPLUS  
DOCUMENT NUMBER: 114:82502  
TITLE: Position 10 is critical for antagonists of the luteinizing hormone-releasing hormone and for inhibition of ovulation in rats  
AUTHOR(S): Feng, Dong Mei; Ljungqvist, Anders; Hook, William A.; Bowers, Cyril Y.; Folkers, Karl  
CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA  
SOURCE: Zeitschrift fuer Naturforschung, B: Chemical Sciences (1990), 45(11), 1567-70  
CODEN: ZNBSEN; ISSN: 0932-0776  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Eleven analogs of LH-RH have been designed, synthesized, bioassayed, and compared for antioviulatory activity in rats. The emphasis of design was on analogs with D-Ala10, Sar10, D-Ser10, (desGly10-NH<sub>2</sub>), D-Abu10 (Abu =

2-aminobutyric acid), Gly10, and with substitutions in position 5, 6, and 8. High antiovolatory activity was obtained with analogs having D-Ala in position 10. Four earlier analogs with D-Ala in position 10 showed 67-100% antiovolatory activity at 0.25  $\mu$ g in rats.

IT 118427-62-6

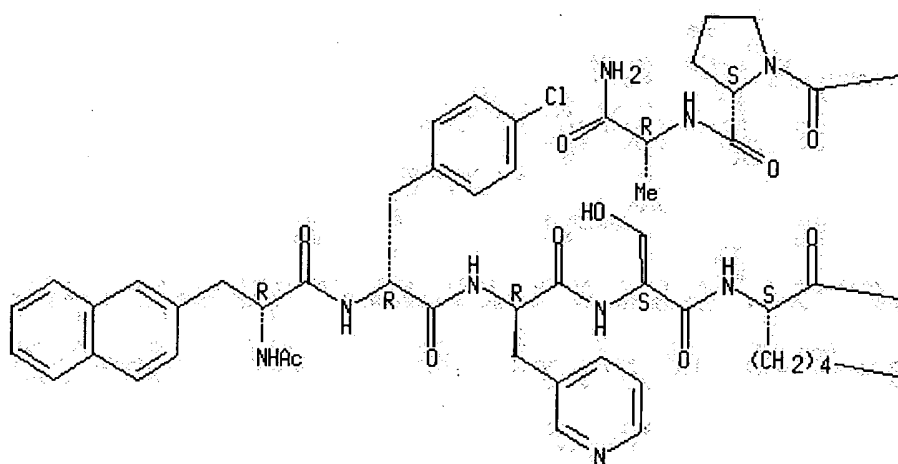
RL: RCT (Reactant); RACT (Reactant or reagent)  
(LH-RH antagonistic activity of)

RN 118427-62-6 HCAPLUS

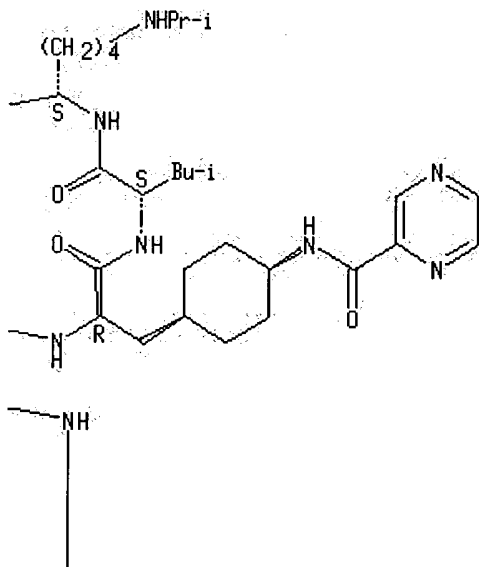
CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N6-(2-pyridinylcarbonyl)-L-lysyl-3-[4-[(pyrazinylcarbonyl)aminocyclohexyl]-D-alanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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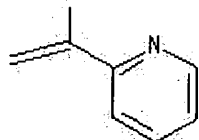
PAGE 1-B



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L8 ANSWER 43 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1990:584857 HCAPLUS  
 DOCUMENT NUMBER: 113:184857  
 TITLE: Antagonists of LHRH superior to antide; effective sequence-activity relationships  
 AUTHOR(S): Ljungqvist, Anders; Feng, Dong Mei; Bowers, Cyril; Hook, William A.; Folkers, Karl  
 CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, USA  
 SOURCE: Tetrahedron (1990), 46(9), 3297-304  
 CODEN: TETRAB; ISSN: 0040-4020  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The antioviulatory (AOA) and histamine-releasing activities of 20 analogs of LH-RH featuring acylated aminocyclohexylalanines and acylated lysines in positions 5 and 6 were studied in rats. (N-Ac-D-2-Nal1,D-pClPhe2,D-3-Pal3,PicLys5,c-D-PzACAla6,Val7,Ilys8,D-Ala10)-LH-RH (100% AOA/0.5 ug) and (N-Ac-D-2-Nal1,D-pPhe2 D-3-Pal,PicLys5,D-Piclys6,Abu7,D-Ala10)-LH-RH (50% AOA/0.25 ug) were the most potent.

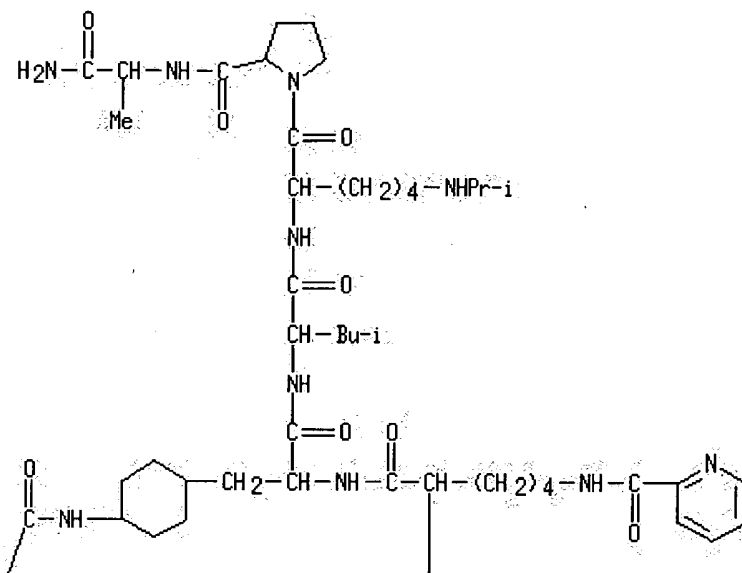
IT 130022-19-4

RL: BIOL (Biological study)  
 (antioviulatory and histamine-releasing activity of, structure in relation to)

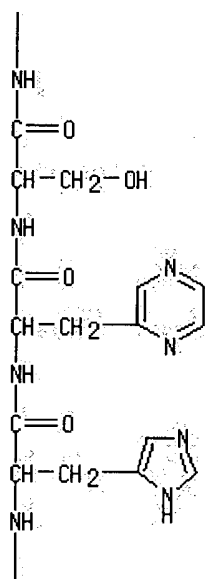
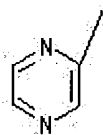
RN 130022-19-4 HCAPLUS

CN D-Alaninamide, 5-oxo-L-prolyl-L-histidyl-3-pyrazinyl-D-alanyl-L-seryl-N6-(2-pyridinylcarbonyl)-L-lysyl-3-[4-[(pyrazinylcarbonyl)amino]cyclohexyl]-D-alanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, cis- (9CI) (CA INDEX NAME)

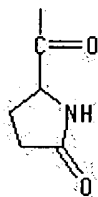
PAGE 1-A



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L8 ANSWER 44 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1990:179888 HCAPLUS

DOCUMENT NUMBER: 112:179888  
 TITLE: Preparation and formulation of linear analogs of atrial natriuretic peptides (ANP)  
 INVENTOR(S): Scarborough, Robert M.; Lewicki, John A.; Johnson, Lorin K.  
 PATENT ASSIGNEE(S): California Biotechnology, Inc., USA  
 SOURCE: PCT Int. Appl., 80 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8905654	A1	19890629	WO 1988-US4638	19881222
W: AU, DK, FI, HU, JP, KR				
AU 8929278	A1	19890719	AU 1989-29278	19881222
ZA 8809598	A	19891025	ZA 1988-9598	19881222
JP 03503048	T2	19910711	JP 1989-501372	19881222
KR 9709887	B1	19970619	KR 1989-71598	19890824
PRIORITY APPLN. INFO.:		US 1987-138893	A	19871224
		US 1988-237299	A	19880826
		US 1988-285916	A	19881216
		WO 1988-US4638	A	19881222

OTHER SOURCE(S): MARPAT 112:179888

AB Z1-Z2-A1-A2-A3-A4-A5-Z3 [I; A1, A4 = basic/noncyclic, neutral/nonpolar/small, or neutral/polar/large/nonarom. amino acid residue, and A1 may addnl. = nonpolar/large/nonarom. amino acid residue; A2 = neutral/nonpolar/large/nonarom. D- or L-amino acid residue; A3 = acidic amino acid residue; A5 = bond, neutral/ nonpolar/large/nonarom. D- or L-amino acid; Z1 = hydrophobic aliph., arom., or mixed aliph./arom. C6-20 org. group, a peptide of 1-125 amino acids; Z2 = 4.5-15 angstrom spacer group; Z3 = OH, (un)substituted NH<sub>2</sub>, peptide of 1-20 amino acids], useful as natriuretics, diuretics, or vasodilators, are prepd. Thus, Q-Gly-Gly-Arg-Ile-Asp-Arg-Ile-Gly-Ala-NH<sub>2</sub> (Q = 2-naphthylacetyl) was prepd. by the solid phase method using BOC-Ala-pMBHA resin (BOC = Me<sub>3</sub>CO<sub>2</sub>C, pMBHA = p-methylbenzhydrylamine). Q1-Arg-Ile-Asp-Arg-NH-(S)-CH<sub>2</sub>CHMeEt [Q1 =  $\alpha$ -[4-(2-naphthoylamino)phenyl]acetyl] in vitro inhibited the binding of 125I-rANPC126-150 to specific receptors on cultured bovine aortic smooth muscle cells or bovine endothelial cells with a binding const. K<sub>i</sub> of 2.52 nM.

IT 124833-20-1P

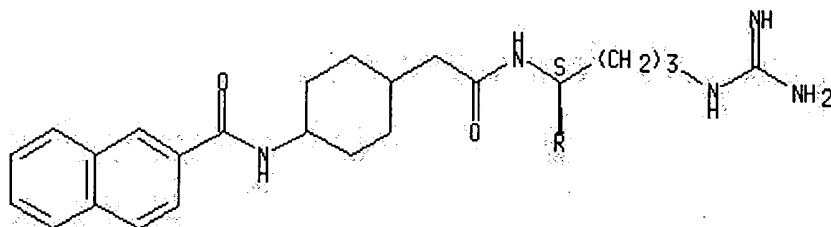
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as natriuretic, diuretic, and vasodilator)

RN 124833-20-1 HCAPLUS

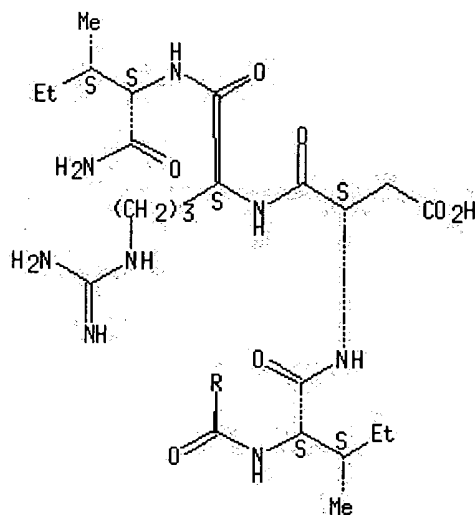
CN L-Isoleucinamide, N2-[[4-[(2-naphthalenylcarbonyl)amino]cyclohexyl]acetyl]-L-arginyl-L-isoleucyl-L- $\alpha$ -aspartyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L8 ANSWER 45 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1990:77959 HCAPLUS  
 DOCUMENT NUMBER: 112:77959  
 TITLE: Preparation of linear analogs of atrial natriuretic peptides as natriuretics, diuretics, or vasodilators  
 INVENTOR(S): Scarborough, Robert M.; Lewicki, John A.; Johnson, Lorin K.  
 PATENT ASSIGNEE(S): California Biotechnology, Inc., USA  
 SOURCE: Eur. Pat. Appl., 57 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 323740	A2	19890712	EP 1988-312221	19881222
EP 323740	A3	19901212		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5047397	A	19910910	US 1988-285916	19881216
ZA 8809598	A	19891025	ZA 1988-9598	19881222
PRIORITY APPLN. INFO.:				
			US 1987-138893	A 19871224
			US 1988-237299	A 19880826
			US 1988-285916	A 19881216
			US 1985-795220	B2 19851105



US 1986-868312	A2 19860528
US 1986-904091	B2 19860904
US 1986-921360	B2 19861028
US 1988-168661	A2 19880316

AB Z1Z2-A1-A2-A3-A4-A5-Z3 [I; A1, A4 = basic/noncyclic, neutral/nonpolar/small, or neutral/polar/large/nonarom. amino acid residue; A1 = neutral/nonpolar/large/nonarom. amino acid residue; A2 = neutral/nonpolar/large/nonarom. D- or L-amino acid residue; A3 = acidic amino acid residue; A5 = neutral/nonpolar/large/nonarom. D- or L-amino acid residue; Z1 = peptide of 1-125 amino acids having its carboxy-terminal residue a hydrophobic amino acid residue or the deamino form, C6-20 hydrophobic aliph., arom., or mixed aliph./arom. org. group; Z1 = spacer group; Z3 = OH, (C1-10 alkylated) amino, peptide of 1-20 amino acids or its (alkyl) amide; provided that when A5 = covalent bond, Z3  $\neq$  OH, NH<sub>2</sub> or peptide; wherein  $\geq 1$  of of the amide linkages between adjacent amino acid residue is replaced by CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>S, CH<sub>2</sub>CH<sub>2</sub>, CH:CH, COCH, CH(OH)CH<sub>2</sub>, or CH<sub>2</sub>SO], which have natriuretic, diuretic and hypotensive activity in mammals and may possess vasorelaxant activity or inhibit the release of aldosterone and renin and thus can be used in the treatment of various edematous states such as congestive heart failure, nephrotic syndrome, hypertension, etc., are prepd. Thus, Q-Gly-Gly-Arg-Ile-Asp-Arg-Ile-Gly-Ala-NH<sub>2</sub> was prepd. by the solid phase synthesis using BOC-Ala-pMBHA (p-methylbenzhydrylamine) resin, protected amino acids, and 2-naphthylacetic acid. In receptor binding assays, I competed with an iodinated native atrial natriuretic peptide (125I-rANP) (II), for binding to receptors from cultured bovine aortic smooth muscle or bovine endothelial cells with K<sub>i</sub>(app) values (the concns. of unlabeled peptide at which 50% of II binding is displaced) of 2.52- >400 nM.

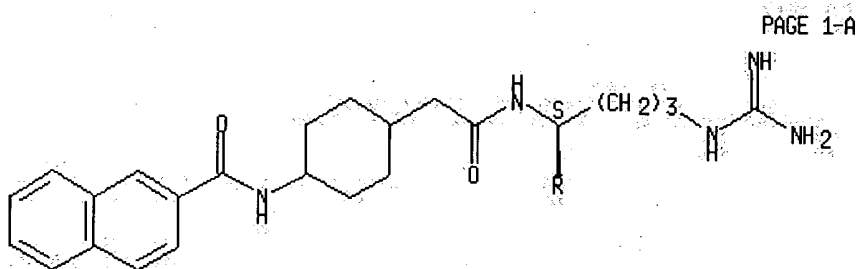
IT 124833-20-1P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as diuretic, natriuretic and vasodilator)

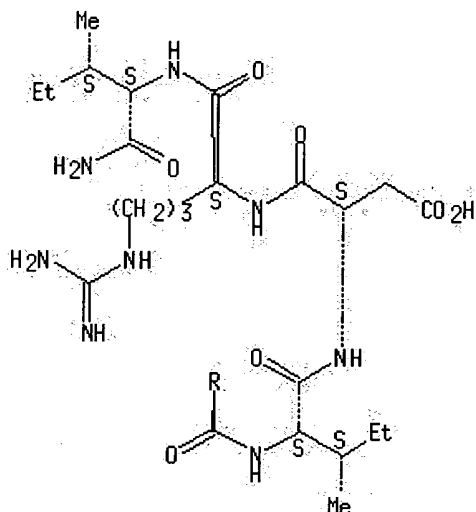
RN 124833-20-1 HCAPLUS

CN L-Isoleucinamide, N2-[[4-[(2-naphthalenylcarbonyl)amino]cyclohexyl]acetyl]-L-arginyl-L-isoleucyl-L- $\alpha$ -aspartyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 2-A



L8 ANSWER 46 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1989:534755 HCAPLUS  
DOCUMENT NUMBER: 111:134755  
TITLE: Preparation of decapeptides as LHRH antagonists having high antioovulatory activity and negligible histamine releasing activity  
INVENTOR(S): Folkers, Karl; Bowers, Cyril Y.; Ljungquist, Anders; Tang, Pui Fun Louisa; Kobota, Minoru; Feng, Dong Mei  
PATENT ASSIGNEE(S): University of Texas System, USA  
SOURCE: PCT Int. Appl., 70 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8901944	A1	19890309	WO 1988-US2922	19880824
W: AT, AU, BB, BG, BR, CH, DE, DK, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
US 4935491	A	19900619	US 1987-88431	19870824
AU 8825294	A1	19890331	AU 1988-25294	19880824
AU 619221	B2	19920123		
EP 377665	A1	19900718	EP 1988-908786	19880824
EP 377665	B1	19950712		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03501969	T2	19910509	JP 1988-507982	19880824
HU 59940	A2	19920728	HU 1988-5868	19880824
HU 213098	B	19970228		
CA 1339659	A1	19980203	CA 1988-587364	19881230
KR 135276	B1	19980423	KR 1989-700699	19890421
DK 9000486	A	19900419	DK 1990-486	19900223
DK 173753	B1	20010910		
NO 9000888	A	19900423	NO 1990-888	19900223
NO 9402179	A	19900423	NO 1994-2179	19940610

## PRIORITY APPLN. INFO.:

US 1987-88431	A2 19870824
WO 1988-US2922	A 19880824
NO 1990-888	A 19900223

OTHER SOURCE(S): CASREACT 111:134755

AB Decapeptide analogs of LHRH, e.g. [N-Ac-D-2-Nal1, D-pClPhe2, D-3-Pal3, NicLys5, D-NicLys6, Ilys8, D-Ala10]-LHRH [2-Nal = 3-(2-naphthyl)alanine, pClPhe = 3-(4-chloro)phenylalanine, 3-Pal = 3-(3-pyridyl)alanine, NicLys = Nε-anisotinoyl, Ilys = Nε-isopropyllysine] (I) (Antide) having high ovulation inhibition activity and very low histamine release activity, were prepd. I and other decapeptides were synthesized by the solid phase method using a Beckman Model 990 peptide synthesizer, new lysine, ornithine, alanine, glutamic acid and arginine derivs., and benzhydrylamine hydrochloride resin as a solid support. I showed antioviulatory activity (AOA) of 100% at 1 µg and 36% at 0.5 µg in rats and an ED50 of ≥300 µg/mL for histamine release in a rat mast cell assay.

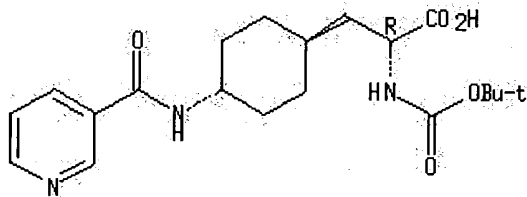
IT 122532-87-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and peptide coupling of, in prepn. of LHRH antagonist)

RN 122532-87-0 HCAPLUS

CN Cyclohexanepropanoic acid, α-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-[(3-pyridinylcarbonyl)amino]-, [1(R)-trans]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 47 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1989:51392 HCAPLUS  
DOCUMENT NUMBER: 110:51392  
TITLE: Antide and related antagonists of luteinizing hormone release with long action and oral activity  
AUTHOR(S): Ljungqvist, Anders; Feng, Dong Mei; Hook, William; Shen, Zong Xuan; Bowers, Cyril; Folkers, Karl  
CORPORATE SOURCE: Inst. Biomed. Res., Univ. Texas, Austin, TX, 78712, USA  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1988), 85(21), 8236-40  
CODEN: PNASA6; ISSN: 0027-8424  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Antide is the decapeptide N-Ac-D-Nal(2), D-Phe(pCl), D-Pal(3), Ser, Lys(Nic), D-Lys(Nic), Leu, Lys(iPr), Pro, D-Ala-NH2 [where Nal(2) represents 3-(2-naphthyl)alanine; Phe(p-Cl) represents 3-(4-chlorophenyl)alanine; Pal(3) represents 3-(3-pyridyl)alanine; Lys(Nic) represents Nε-nicotinoyllysine; Lys(iPr) represents Nε-isopropyllysine], which is an antagonist of LH-RH, which has high antioviulatory activity, releases negligible histamine, and is scheduled for scale-up, safety testing, and evaluation in the exptl. primate and in clin. medicine. Twenty-six synthetic peptides, designed on antide with

variations in positions 5-8, were compared with antide for antiovolatory and histamine-releasing activities. Of these, N-Ac-D-Nal(2), D-Phe(pCl), D-Pal(3), Ser, Lys(Pic), cis-D-Ala(PzAC), Leu, Lys(iPr), Pro, D-Ala-NH<sub>2</sub> [where Lys(Pic) represents N $\epsilon$ -picoloyllysine; Ala(PzAC) represents 3-(4-pyrazinylcarbonylamino)cyclohexylalanine] was not only the most potent but also had higher antiovolatory activity than antide, i.e., 73% per 0.25  $\mu$ g and 100% per 0.5  $\mu$ g vs. 36% per 0.5  $\mu$ g and 100% per 1.0  $\mu$ g. Antide showed significant duration of action when injected at a dose of 10  $\mu$ g 44 h before injection of 50 ng of the agonist [D-Qal(3)6]LH-RH [where Qal(3) represents 3-(3-quinolyl)alanine]. Antide showed oral antiovolatory activity at 600  $\mu$ g (73%) and at 1200  $\mu$ g (100%) with negligible difference between water and corn oil oral formulations.

## IT 118427-58-0

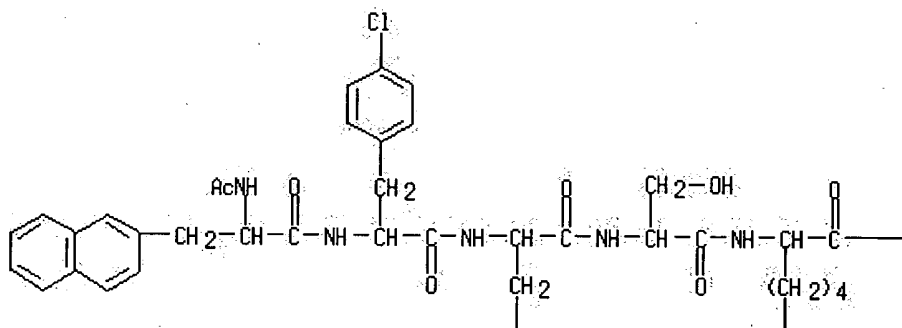
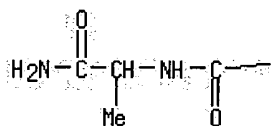
RL: BIOL (Biological study)

(antiovolatory and histamine-releasing activities of, structure in relation to)

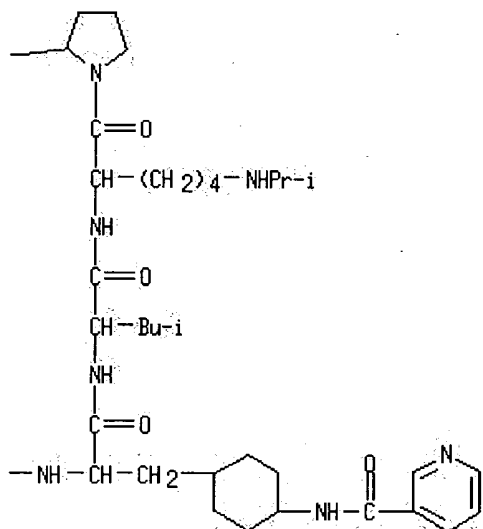
RN 118427-58-0 HCAPLUS

CN D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-N6-(3-pyridinylcarbonyl)-L-lysyl-3-[4-[(3-pyridinylcarbonyl)amino]cyclohexyl]-D-alanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl-, trans- (9CI) (CA INDEX NAME)

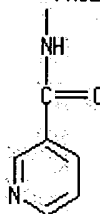
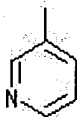
PAGE 1-A



PAGE 1-B



PAGE 2-A



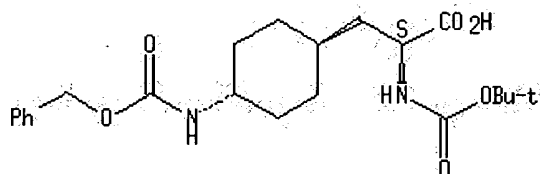
L8 ANSWER 48 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1987:67654 HCAPLUS  
 DOCUMENT NUMBER: 106:67654  
 TITLE: Novel conformationally constrained amino acids as lysine-9 substitutions in somatostatin analogs  
 AUTHOR(S): Nutt, Ruth F.; Curley, Paul E.; Pitzenberger, Steven M.; Freidinger, Roger M.; Saperstein, Richard; Veber, Daniel F.  
 CORPORATE SOURCE: Merck Sharp & Dohme Res. Lab., West Point, PA, 19486, USA  
 SOURCE: Pept.: Struct. Funct., Proc. Am. Pept. Symp., 9th (1985), 441-4  
 CODEN: 54ZNAJ  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English  
 AB Somatostatin cyclohexapeptide analogs cyclo(D-Trp-X-Tyr-Phe-Pro-Phe) (I; X = cis- or trans-4-aminocyclohexylglycine or -alanine residue, p-aminomethylphenylalanine residue) were prepd. and their activities as inhibitors of insulin, glucagon, and growth hormone release were examd. I (X = trans-p-aminomethylphenylalanine) is 10 times more active than I (X = Lys). The results were discussed in terms of their conformations, which were detd. by CD and NMR.  
 IT 98044-59-8P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. and peptide coupling of)  
 RN 98044-59-8 HCAPLUS

CN Cyclohexanepropanoic acid,  $\alpha$ -[[[(1,1-dimethylethoxy)carbonyl]amino]-4-  
[[[(phenylmethoxy)carbonyl]amino]-, [1(S)-trans]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

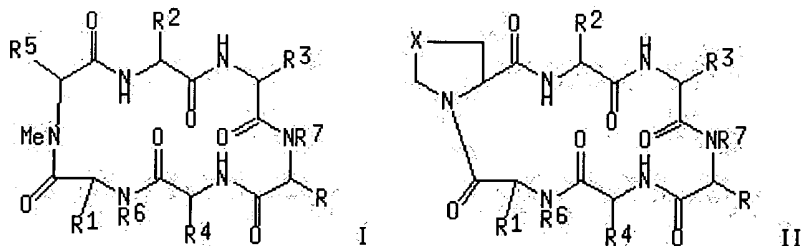


L8 ANSWER 49 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1985:523923 HCAPLUS  
DOCUMENT NUMBER: 103:123923  
TITLE: Cyclic hexapeptide somatostatin analogs and their use  
INVENTOR(S): Nutt, Ruth F.  
PATENT ASSIGNEE(S): Merck and Co., Inc., USA  
SOURCE: Eur. Pat. Appl., 38 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 143307	A2	19850605	EP 1984-112488	19841017
EP 143307	A3	19860507		
EP 143307	B1	19890104		
R: CH, DE, FR, GB, IT, LI, NL				
US 4522813	A	19850611	US 1983-545982	19831027
JP 60109600	A2	19850615	JP 1984-225155	19841027
PRIORITY APPLN. INFO.: GI			US 1983-545982	19831027



AB Title cyclic hexapeptides I and II [R = (CH<sub>2</sub>)<sub>m</sub>Y(CH<sub>2</sub>)<sub>p</sub>NH<sub>2</sub> (m = 0, 1; p = 0, Y = cyclohexylene; p = 1, Y = phenylene); R<sub>1</sub>, R<sub>2</sub> = (un)substituted alkyl or benzyl; R<sub>3</sub> = (un)substituted indol-3-ylmethyl; R<sub>4</sub> = alkyl, hydroxyalkyl, carboxyalkyl, aminoalkyl, indol-3-ylmethyl, (un)substituted benzyl; R<sub>5</sub> = alkyl, (un)substituted benzyl; R<sub>6</sub>, R<sub>7</sub> = H, Me; X = (CH<sub>2</sub>)<sub>n</sub> (n = 0, 1, 2), S] were prepd. as inhibitors of the release of growth hormone (GH), insulin, glucagon, and gastric acid secretions. Thus, H-D-Trp-AChxAla(Z)-Thr(CH<sub>2</sub>Ph)-Phe-Pro-Phe-O-resin (AChxAla = 4-aminocyclohexylalanine residue, Z = CO<sub>2</sub>CH<sub>2</sub>Ph) was prepd. by the solid-phase method and then it was resin cleaved by NH<sub>2</sub>NH<sub>2</sub> to give H-D-Trp-AChxAla(Z)-Thr(CH<sub>2</sub>Ph)-Phe-Pro-Phe-NHNH<sub>2</sub>. The latter was cyclized

by the azide method to give cyclo[D-Trp-AChxAla(Z)-Thr(CH<sub>2</sub>Ph)-Phe-Pro-Phe], which was deblocked by HF/anisole to give cyclo(D-Trp-AChxAla-Thr-Phe-Pro-Phe) (III). The in vitro activity of III for the inhibition of GH release in rat pituitaries was 1.3 as compared to a value of 1 for somatostatin. III also inhibited gastric secretion in dogs.

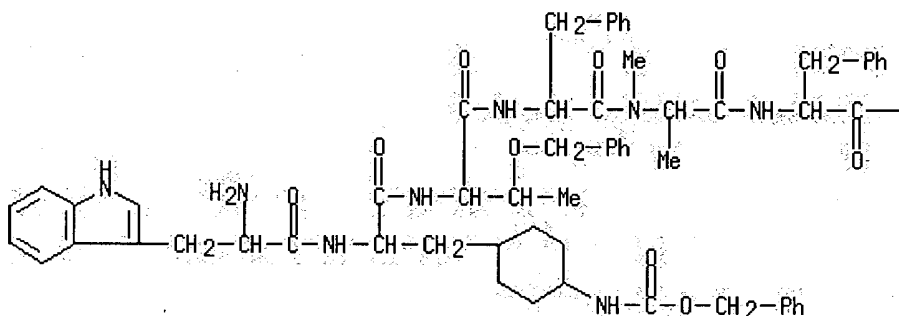
IT 98044-64-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and conversion of, to azide)

RN 98044-64-5 HCAPLUS

CN L-Phenylalanine, N-[N-methyl-N-[N-[N-[3-[4-[(phenylmethoxy)carbonyl]amino]cyclohexyl]-N-D-tryptophyl-L-alanyl]-O-(phenylmethyl)-L-threonyl]-L-phenylalanyl]-L-alanyl-, hydrazide, trans- (9CI) (CA INDEX NAME)

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-NH-NH<sub>2</sub>

L8 ANSWER 50 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1983:46436 HCAPLUS

DOCUMENT NUMBER: 98:46436

TITLE: Search for antineoplastic agents among  
4- [bis(2-chloroethyl)amino]cyclohexylacetic acid  
derivatives

AUTHOR(S): Prasmickiene, G.; Grazeliene, G.; Karpavicius, K.

CORPORATE SOURCE: USSR

SOURCE: Izuch. Funkts. Kletki (1981), 35-41. Editor(s):  
Kanopkaite, S. I. Inst. Biokhim. Akad. Nauk Lit. SSR:  
Vilnius, USSR.

CODEN: 48RBAS

DOCUMENT TYPE: Conference

LANGUAGE: Russian

GI



AB 4- [Bis(2-chloroethyl)amino]cyclohexylacetic acid derivs. I [R = OH, OEt, NHCH(CO<sub>2</sub>H)CH<sub>2</sub>Ph, or NHCH(CO<sub>2</sub>H)CHMe<sub>2</sub>] and I N-oxide (R = OEt) [83661-88-5] were tested for antitumor activity and toxicity. In vitro-in vivo sarcoma

45 in rats was completely inhibited by I-HCl (R = OH) [83661-86-3] and I (R = OEt) [83661-87-4], and was 80-90% inhibited by I-HCl (R = NHCH(CO<sub>2</sub>H)CH<sub>2</sub>Ph) [83680-80-2] and I (R = NHCH(CO<sub>2</sub>H)CHMe<sub>2</sub>) [83729-92-4]. However, this activity was not reflected by their in vivo activities. Structure-activity relations are discussed.

IT 83680-80-2

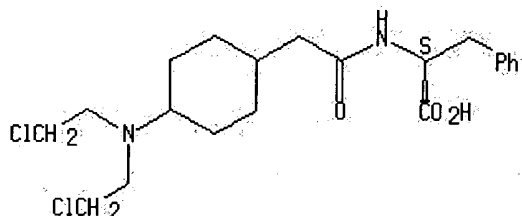
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(neoplasm-inhibiting activity of, structure in relation to)

RN 83680-80-2 HCAPLUS

CN L-Phenylalanine, N-[[4-[bis(2-chloroethyl)amino]cyclohexyl]acetyl]- (9CI)  
(CA INDEX NAME)

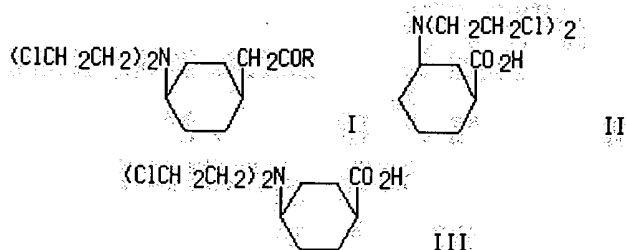
Absolute stereochemistry.



L8 ANSWER 51 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:	1981:481445 HCAPLUS
DOCUMENT NUMBER:	95:81445
TITLE:	Synthesis of bis(2-chloroethyl)aminocyclohexylcarboxylic (acetic) acids and their derivatives
AUTHOR(S):	Karpavicius, K.; Prasmickiene, G.; Palaima, A.; Knunyants, I. L.
CORPORATE SOURCE:	Inst. Elementoorg. Soedin. im. Nesmeyanova, Moscow, USSR
SOURCE:	Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1981), (1), 165-9 CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE:	Journal
LANGUAGE:	Russian
OTHER SOURCE(S):	CASREACT 95:81445
GI	



AB Condensing H-DL-Phe-OCH<sub>2</sub>Ph with cis-4-[bis(2-chloroethyl)amino]cyclohexane acetic acid hydrochloride in CHCl<sub>3</sub> contg. dicyclohexylcarbodiimide gave the cyclohexylacetyl amino acid I (R = DL-Phe-OCH<sub>2</sub>Ph), which underwent hydrogenolysis in the presence of Pd/C to give I (R = DL-Phe-OH). I (R = DL-Leu-OH) was prepd. similarly. Chloroethylcyclohexanecarboxylic acids II and III were also prepd.

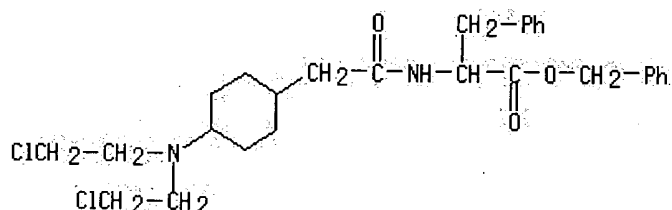


IT 78609-69-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and hydrogenolysis of)

RN 78609-69-5 HCAPLUS

CN Phenylalanine, N-[[cis-4-[bis(2-chloroethyl)amino]cyclohexyl]acetyl]-, phenylmethyl ester, monohydrochloride (9CI) (CA INDEX NAME)



# HCl

L8 ANSWER 52 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1981:16033 HCAPLUS

DOCUMENT NUMBER: 94:16033

TITLE: Phenylalanine derivatives containing an acyl residue of stereoisomeric N-(diethylenimidothiophosphoryl)-4-aminocyclohexylacetic acids

AUTHOR(S): Patockiene, L.; Karpavicius, K.; Knunyants, I. L.

CORPORATE SOURCE: Inst. Elementoorg. Soedin., Moscow, USSR

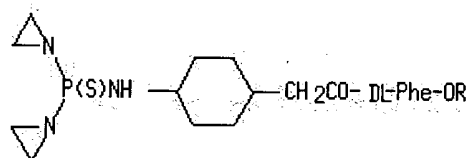
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1980), (6), 1426-8

CODEN: IASKA6; ISSN: 0002-3353

DOCUMENT TYPE: Journal

LANGUAGE: Russian

GI



I

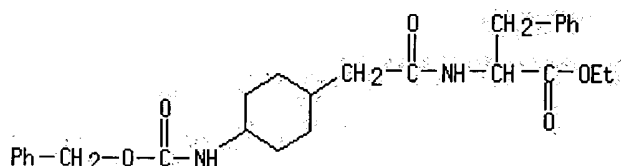
AB Cis and trans isomers of the title compd. I (R = Et, Na) were prepd. via peptide coupling reactions of 4-(benzyloxycarbonylamino)cyclohexylacetic acid isomers with DL-Phe-OEt.

IT 75695-18-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. and deblocking of)

RN 75695-18-0 HCAPLUS

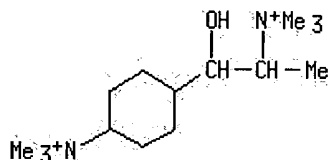
CN Phenylalanine, N-[[cis-4-[[[(phenylmethoxy)carbonyl]amino]cyclohexyl]acetyl]-, ethyl ester (9CI) (CA INDEX NAME)



L8 ANSWER 53 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1977:608489 HCAPLUS  
DOCUMENT NUMBER: 87:208489  
TITLE: Studies on the occurrence of hydrogen transfer, 44. Enantioselective electroreduction of Schiff's bases using optically active supporting electrolytes  
AUTHOR(S): Horner, Leopold; Skaletz, Detlef H.  
CORPORATE SOURCE: Inst. Org. Chem., Univ. Mainz, Mainz, Fed. Rep. Ger.  
SOURCE: Justus Liebig's Annalen der Chemie (1977), (8), 1365-409  
CODEN: JLACBF; ISSN: 0075-4617  
DOCUMENT TYPE: Journal  
LANGUAGE: German  
AB Prochiral Schiff's bases were electrochem. reduced to the corresponding 1,2-diamine dimer and secondary amine using a series of 36 optically active electrolytes. The former products were optically inactive, the latter however show optical induction of  $\leq 11\%$ . In the redn. of acetophenone [98-86-2] and of N-( $\alpha$ -methylbenzylidene)benzylamine [14428-98-9], using either derivs. of ephedrine, pseudoephedrine or deoxyephedrine as electrolyte, enantiomers with the same configuration are produced in comparable optical yield. The enantioselective electrochem. redn. of prochiral Schiff's bases using optically active  $\alpha$ -methylbenzylamine derivs. as electrolyte was systematically studied as a function of structure. The effect of variations in electrolyte concn. and optical purity, temp., pH, cathode potential, c. d. and solvent were established. In the case of (+)-(S)-N-( $\alpha$ -methylbenzylidene)- $\alpha$ -methylbenzylamine, the contributions from internal and external asym. induction were studied. The enantioselectivities of the electroredn., catalytic hydrogenation, and redn. with complex metal hydrides were studied for several suitable substrates. The electrochem. optical induction in the case of the redn. of Schiff's bases is regarded as a consequence of an interconformational interaction between substrate and electrolyte, and this effect was investigated and interpreted with respect to changes in substrate type, structure and configuration. A specifically adsorbed electrolyte (shown by a.c. polarog.) is assumed to interact with the substrate, leading to an ionic transition state with charge-transfer character, in which H bonding is also important. Cyclic electrolytes, whose conformational mobility is drastically reduced with respect to the corresponding open-chain analogs, show an enantioselectivity for the same abs. configuration but with reduced optical yield. The highest optical inductions were obsd. with certain diquatary salts.  
IT 64868-24-2  
RL: PRP (Properties)  
(electroredn. of Schiff bases in presence of supporting electrolytes of)  
RN 64868-24-2 HCAPLUS  
CN Cyclohexaneethanaminium,  $\beta$ -hydroxy-N,N,N, $\alpha$ -tetramethyl-4-(trimethylammonio)-, diiodide, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

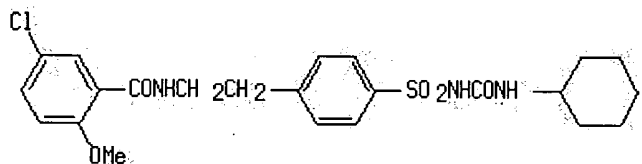


# 2 I-

L8 ANSWER 54 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1976:503654 HCAPLUS  
 DOCUMENT NUMBER: 85:103654  
 TITLE: Radioimmunoassay for glyburide in human serum  
 AUTHOR(S): Royer, Max E.; Ko, Howard; Evans, J. S.; Johnston, Karen T.  
 CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, USA  
 SOURCE: Analytical Letters (1976), 9(7), 629-40  
 CODEN: ANALBP; ISSN: 0003-2719  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB A radioimmunoassay to measure ng amts. of glyburide (Micronase) (I) [10238-21-8] is described. Of the compds. tested, only the known hydroxy metabolites of I cross-reacted significantly. Using 20  $\mu$ l specimens, contg. 25.6 ng I/ml serum, the within-day and between-day coeffs. of variation for the assay were 3.47% and 3.18%, resp. Recoveries were quant. (100.6%). In normal human volunteers, peak serum drug concns. were obsd. at 4.3 hr. After single oral doses of I (1.25-5 mg), measurable amts. of drug-related materials were found in serum at 24 hr post-drug administration.

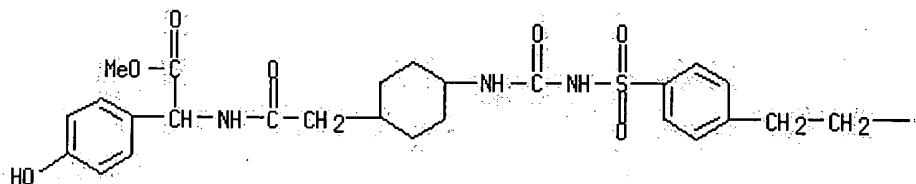
IT 60450-84-2

RL: BIOL (Biological study)  
 (cross reaction with antibody to glyburide)

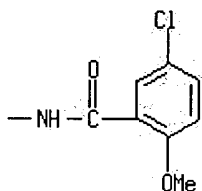
RN 60450-84-2 HCAPLUS

CN Benzeneacetic acid,  $\alpha$ -[[[4-[[[[[4-[2-[(5-chloro-2-methoxybenzoyl)amino]ethyl]phenyl]sulfonyl]amino]carbonyl]amino]cyclohexyl]acetyl]amino]-4-hydroxy-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



L8 ANSWER 55 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1967:46510 HCAPLUS  
 DOCUMENT NUMBER: 66:46510  
 TITLE: Examination of lobinaline and some degradation products by mass spectrometry  
 AUTHOR(S): Clugston, D. M.; MacLean, David Bailey; Manske, Richard H. F.  
 CORPORATE SOURCE: McMaster Univ., Hamilton, Can.  
 SOURCE: Canadian Journal of Chemistry (1967), 45(1), 39-47  
 CODEN: CJCHAG; ISSN: 0008-4042  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

GI For diagram(s), see printed CA Issue.

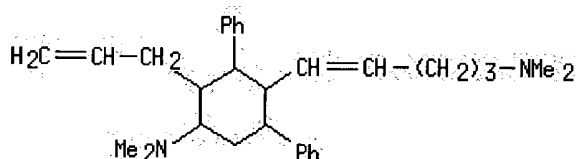
AB Lobinaline (I), its derivs., and its Hofmann degradation products were examd. by mass spectrometry and other spectral and chem. techniques. The results provide independent evidence for the structure of the alkaloid, but indicate that the free base may exist as a mixt. of two or three tautomers.

IT 14028-80-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 14028-80-9 HCAPLUS

CN Cyclohexylamine, 2-allyl-4-[5-(dimethylamino)-1-pentenyl]-N,N-dimethyl-3,5-diphenyl- (8CI) (CA INDEX NAME)



L8 ANSWER 56 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1957:5485 HCAPLUS  
 DOCUMENT NUMBER: 51:5485  
 ORIGINAL REFERENCE NO.: 51:1169d-i, 1170a-g  
 TITLE: Hexamethylene-1,6-bis[tertiary-amines] in which part of the six carbon chain is also part of a six-membered ring  
 AUTHOR(S): McMillan, Freeman H.; Kun, Kenneth A.; McMillan, Carol B.; King, John A.  
 CORPORATE SOURCE: Warner-Chilcott Research Labs., New York, NY  
 SOURCE: Journal of the American Chemical Society (1956), 78, 4077-81  
 CODEN: JACSAT; ISSN: 0002-7863  
 DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

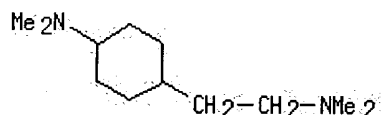
AB 4-(3-Hydroxypropyl)pyridine (I) (137 g.) in 1200 cc. Me<sub>2</sub>CO contg. 125 g. MeBr and the mixt. kept at 30° overnight gave 199 g. I.MeBr, m. 78-80° (from EtOH-Me<sub>2</sub>CO). I.MeBr (174 g.) in 700 cc. EtOH hydrogenated at 60° and 800 lb., cooled, filtered, and evapd. in vacuo on the steam bath yielded 150 g. 1-methyl-4-(3-hydroxypropyl)piperidine-HBr (II), m. 117-18° (from 600 cc. 1:3 EtOH-Me<sub>2</sub>CO). II (17 g.) in 60 cc. EtOH contg. 18 g. Me<sub>2</sub>NH heated 1.5 hrs. at 82° in a pressure bottle, cooled, and evapd. to dryness in vacuo on the steam bath yielded 6.0 g. 1-methyl-4-(3-dimethylaminopropyl)piperidine-2H Cl (III), m. 245-6° (decompn.) (from 1:2 EtOH-Me<sub>2</sub>CO). I (137 g.) in 1600 cc. H<sub>2</sub>O contg. 65 g. H<sub>2</sub>SO<sub>4</sub> treated slowly with stirring at about 50° with 211 g. KMnO<sub>4</sub>, the mixt. warmed to 80° and filtered, and the filtrate concd. to 500 cc. and cooled gave 92 g. 3-(4-pyridyl)propionic acid (IV), m. 221-4° (from H<sub>2</sub>O). IV (75.5 g.) in slightly more than 0.5 mole 25% aq. Me<sub>2</sub>NH heated until most of the H<sub>2</sub>O had evapd., the acid soln. bubbled slowly 14 hrs. at 210° with Me<sub>2</sub>NH, the mixt. cooled and triturated with 200 cc. C<sub>6</sub>H<sub>6</sub> and filtered, and the filtrate evapd. on the steam bath gave 35 g. N,N-dimethylamide (V) of IV, b<sub>0.35</sub> 143.5-5°. V (21.5 g.) in 80 cc. Me<sub>2</sub>CO kept several hrs. with 24 g. MeBr in a pressure bottle gave 22 g. V.MeBr, m. 113.5-15.5° (from Me<sub>2</sub>CO-EtOH). V.MeBr (9.5 g.) in 100 cc. H<sub>2</sub>O hydrogenated under ambient conditions over 0.25 g. PtO<sub>2</sub> gave 8 g. 1-methyl-4-(2-dimethylamidoethyl)piperidine-2HBr (VI), m. 134-5° (from Me<sub>2</sub>CO). VI (8 g.) added to 30 cc. 30% aq. K<sub>2</sub>CO<sub>3</sub>, the org. layer sepd., the aq. layer extd. with C<sub>6</sub>H<sub>6</sub>, the combined org. layer and ext. dried and evapd., the residual oil (5.5 g.) dissolved in 25 cc. dry C<sub>6</sub>H<sub>6</sub>, the soln. added during 15 min. at room temp. with stirring to 1.9 g. LiAlH<sub>4</sub> in 100 cc. dry Et<sub>2</sub>O, the mixt. refluxed 2 hrs., treated slowly with cooling with 8.8 g. EtOAc and then 10.7 g. NH<sub>4</sub>Cl in 30 cc. H<sub>2</sub>O and stirred with cooling at 0° while being treated with solid Na<sub>2</sub>SO<sub>4</sub>, and the org. layer treated with a slight excess of HCl in EtOH yielded 1.5 g. III, m. 254-5° (decompn.). p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H (181 g.) and 300 g. SOCl<sub>2</sub> refluxed 2 hrs. and evapd. in vacuo, the residue dissolved in 200 cc. C<sub>6</sub>H<sub>6</sub>, the soln. added dropwise to 100 g. Me<sub>2</sub>NH in 500 cc. C<sub>6</sub>H<sub>6</sub> below 10°, the mixt. refluxed 1 hr. and filtered hot, and the filtrate chilled gave 87.5 g. p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONMe<sub>2</sub> (VII), m. 88-90°. VII (85 g.) in 800 cc. EtOH hydrogenated at 25° over 1.0 g. PtO<sub>2</sub> gave 58 g. p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONMe<sub>2</sub> (VIII), m. 98-100°. VIII (32 g.), 0.5 g. PtO<sub>2</sub>, 15.1 cc. concd. HCl, 26.6 g. 40% aq. CH<sub>2</sub>O, and 100 cc. 95% EtOH hydrogenated at 25° and 3 atm., the mixt. filtered, the filtrate evapd. to dryness in vacuo, the residue dissolved in 100 cc. H<sub>2</sub>O, the soln. basified strongly with 50% aq. NaOH and extd. with 100 cc. C<sub>6</sub>H<sub>6</sub>, the ext. treated with 10 cc. Ac<sub>2</sub>O, warmed 15 min. on the steam bath, cooled, shaken with 100 cc. 10% aq. NaOH, and extd. with 125 cc. 1:4 dil. HCl, the acidic ext. basified with 50% aq. NaOH and extd. with C<sub>6</sub>H<sub>6</sub>, and the ext. worked up gave 30 g. p-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CONMe<sub>2</sub> (IX), b<sub>0.1</sub> 125-30°, m. 78-9°. IX (10.3 g.) in 250 cc. Et<sub>2</sub>O added to 1.9 g. LiAlH<sub>4</sub> in 100 cc. Et<sub>2</sub>O, the mixt. refluxed 0.5 hr., cooled, treated with 13.2 g. EtOAc and then with 10.7 g. NH<sub>4</sub>Cl in 35 cc. H<sub>2</sub>O, and the Et<sub>2</sub>O layer worked up gave 9.0 g. p-Me<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>N Me<sub>2</sub> (X), b<sub>0.05</sub> 72-5°. X (9.0 g.) in 100 cc. abs. EtOH treated with 8.5 cc. concd. HCl and dild. with 100 cc. abs. Et<sub>2</sub>O gave 10.6 g. X.H Cl, m. 227-8° (decompn.). X (16.5 g.) in 130 g. glacial AcOH hydrogenated 48 hrs. at 25° and 1 atm. over 1.0 g. PtO<sub>2</sub> yielded 11.5 g. 1-dimethylamino-4-(2-dimethylaminoethyl)cyclohexane (XI), m. 280° (decompn.). p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H was converted similarly to 56% p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>CONMe<sub>2</sub>, m. 63.5-4.5° (from 1:1 C<sub>6</sub>H<sub>6</sub>-ligroine, b. 60-80°). Diacid chloride of trans-cyclohexane-1,4-dicarboxylic acid (XII) (41.8 g.) in 100 cc. dry C<sub>6</sub>H<sub>6</sub> added slowly below 20° to

58 g. Me<sub>2</sub>NH in 300 cc. dry C<sub>6</sub>H<sub>6</sub>, the mixt. warmed and filtered hot, and the filtrate chilled yielded 12.5 g. 1,4-trans-bis(dimethylcarbamoyl)cyclohexane (XIII), m. 201° (from C<sub>6</sub>H<sub>6</sub>), which hydrogenated yielded 57%, 1,4-trans-bis(dimethylaminomethyl)cyclohexane (XIV), b0.03 62°, m. 35°; 37% di-HCl salt, m. 309-10°. Similarly were prepd. 33% cis isomer of XIII, m. 123-3.5°; and the cis isomer of XIV, b0.05 58° (di-HCl salt, m. 290°). m-HO<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H (39 g.) and 150 cc. SOCl<sub>2</sub> refluxed 1 hr. and evapd. in vacuo on the steam bath, the residue in 150 cc. dry C<sub>6</sub>H<sub>6</sub> added slowly below 20° to 45 g. Me<sub>2</sub>NH in 300 cc. dry C<sub>6</sub>H<sub>6</sub>, the mixt. cooled, and filtered, and the filtrate washed with 30% aq. K<sub>2</sub>CO<sub>3</sub> and distd. gave 33 g. m-Me<sub>2</sub>NOCC<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>CONMe<sub>2</sub>, m. 88-90°, b0.1 170-5°, which reduced gave 59% m-Me<sub>2</sub>NCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>)<sub>2</sub>NMe<sub>2</sub>, b0.05 68° (50 % di-HCl salt, m. 253-5°). In the same manner were prepd. 54% o-C<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>CONMe<sub>2</sub>)<sub>2</sub>, m. 160.5-61° (from C<sub>6</sub>H<sub>6</sub>); 68% o-C<sub>6</sub>H<sub>4</sub>(CH<sub>2</sub>CH<sub>2</sub>NMe<sub>2</sub>)<sub>2</sub>, b0.05 85° (81% di-HCl salt, m. 233°); 55% 1,2-bis(2-dimethylaminoethyl)cyclohexane-2HCl, m. 240-2°. Isocinchomeric acid (100 g.) and 500 g. SOCl<sub>2</sub> refluxed 16 hrs., filtered, and evapd. to dryness in vacuo on the steam bath, the residue dissolved in 250 cc. dry C<sub>6</sub>H<sub>6</sub>, the soln. added slowly below 20° to 162 g. Me<sub>2</sub>NH in 700 cc. dry C<sub>6</sub>H<sub>6</sub>, the mixt. refluxed a few min. and filtered hot, and the filtrate chilled yielded 72 g. bisdimethylamide of isocinchomeric acid (XV), m. 139.5-40.5° (from 500 cc. C<sub>6</sub>H<sub>6</sub>), which was reduced further to 10% 2,5-bis(2-dimethylaminoethyl)pyridine (XVI), b0.07 84° (36% di-HCl salt, m. 265°), and 35% piperidine analog of XVI, b0.05 60° (66% tri-HCl salt, m. 266°) (all HCl salts melted with decompn.). XV (11.1 g.) in 50 cc. Me<sub>2</sub>CO contg. 9.0 g. MeBr kept 16 hrs. at 65° in a pressure bottle gave 24 g. XV.MeBr, m. 158-61° (from EtOH-Et<sub>2</sub>O). XV.MeBr (24 g.) in 100 cc. abs. EtOH hydrogenated about 16 hrs. over 1.0 g. PtO<sub>2</sub> and filtered, the filtrate evapd. in vacuo on the steam bath, the residue in 10 cc. H<sub>2</sub>O treated with 50 g. K<sub>2</sub>CO<sub>3</sub> in 75 cc. H<sub>2</sub>O, the mixt. extd. with C<sub>6</sub>H<sub>6</sub>, and the ext. worked up gave 10 g. 1-methyl-2,5-bis(dimethylcarbamoyl)piperidine, b0.02 145-50°.

IT 105337-96-0, Cyclohexaneethylamine, 4-dimethylamino-N,N-dimethyl-, dihydrochloride  
(prepn. of)

RN 105337-96-0 HCAPLUS

CN Cyclohexaneethylamine, 4-dimethylamino-N,N-dimethyl-, dihydrochloride  
(6CI) (CA INDEX NAME)



# 2 HCl

=> file caold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
294.75	452.90

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-40.19	-40.19

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 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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 L2 1 S L1  
 L3 STRUCTURE UPLOADED  
 L4 1 S L3  
 L5 281 S L3 FULL

FILE 'HCAPLUS' ENTERED AT 03:50:26 ON 26 APR 2004

L6 58 S L5  
 L7 2 S L6 AND ACKERMANN, J?/AU  
 L8 56 S L6 NOT L7  
 L9 0 S L8 AND AEBI, J?/AU  
 L10 0 S L8 AND BLUM, D?/AU  
 L11 0 S L8 AND CHUCHOLOWSKI, A?/AU  
 L12 0 S L8 AND DEHMLow, H?/AU  
 L13 0 S L8 AND MAERKI, H?/AU  
 L14 0 S L8 AND MORAND, O?/AU  
 L15 0 S L8 AND TRUSSARDI, R?/AU  
 L16 0 S L8 AND VON DER MARK, E?/AU  
 L17 0 S L8 AND WALLBAUM, S?/AU  
 L18 0 S L8 AND WELLER, T?/AU

FILE 'CAOLD' ENTERED AT 03:54:56 ON 26 APR 2004

=> s 15

L19 3 L5

=> d 119, 1-3

L19 ANSWER 1 OF 3 CAOLD COPYRIGHT 2004 ACS on STN  
 AN CA51:5015a CAOLD  
 TI bisquaternary ammonium salts - (II) salts of 4,4'-diaminostilbene-2,2'-disulfonic acid  
 AU Leeds, William G.; Slack, R.  
 IT 81-11-8 2079-78-9 21510-10-1 51464-74-5 93840-59-6 108923-06-4

109189-07-3 109220-13-5 119641-55-3 120174-92-7 120548-64-3 121599-60-8  
121848-41-7 122678-97-1 122802-57-7 124115-64-6

L19 ANSWER 2 OF 3 CAOLD COPYRIGHT 2004 ACS on STN

AN CA51:1169d CAOLD

TI hexamethylene-1,6-bis(tertiary-amines) in which part of the sex C chain is also part of a six-membered ring

AU McMillan, Freeman H.; Kun, K. A.; McMillan, C. B.; King, J. A.

IT 125-64-4 497-89-2 6318-43-0 27579-36-8 52780-78-6 81709-36-6  
90405-67-7 99169-50-3 99841-58-4 100248-29-1 100401-56-7 100543-21-3  
100875-76-1 101098-50-4 103798-03-4 103856-36-6 105105-32-6 105337-96-0  
105640-34-4 105904-82-3 105904-83-4 106037-79-0 106274-79-7 106593-56-0  
106841-93-4 107663-02-5 108153-26-0 108302-08-5 108900-73-8 109189-05-1  
109965-30-2 117885-14-0 120207-48-9 131762-74-8

L19 ANSWER 3 OF 3 CAOLD COPYRIGHT 2004 ACS on STN

Full  
Text

AN CA51:481e CAOLD

TI bis(quaternary ammonium salts)

PA May & Baker Ltd.

DT Patent

TI bisquaternary ammonium salts

AU Slack, Ronald

DT Patent

PATENT NO.      KIND              DATE

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PI GB 748224

IT 2079-78-9 21510-10-1 101729-46-8 103031-54-5 109220-13-5 109447-63-4  
116568-23-1 117986-01-3 119641-55-3 120090-06-4 120174-92-7 120548-64-3  
121599-60-8 121791-89-7 121848-41-7 122802-57-7

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ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 109220-13-5 REGISTRY

CN (1,4-Cyclohexyleneethylene)bis[trimethylammonium chloride] (6CI) (CA INDEX NAME)

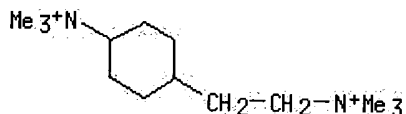
MF C14 H32 N2 . 2 Cl

SR CAOLD

LC STN Files: BEILSTEIN\*, CAOLD

(\*File contains numerically searchable property data)

CRN (122802-56-6)



# 2 Cl<sup>-</sup>

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)



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=> fil reg; d acc 122802-57-7; fil CAOLD

FILE 'REGISTRY' ENTERED AT 03:55:45 ON 26 APR 2004

ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 122802-57-7 REGISTRY

CN (1,4-Cyclohexyleneethylene)bis[trimethylammonium] 4,4'-diamino-2,2'-stilbenedisulfonate (6CI) (CA INDEX NAME)

MF C14 H32 N2 . C14 H12 N2 O6 S2

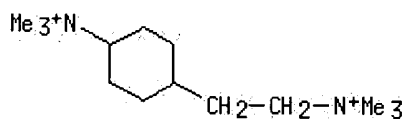
SR CAOLD

LC STN Files: BEILSTEIN\*, CAOLD  
(\*File contains numerically searchable property data)

CM 1

CRN 122802-56-6

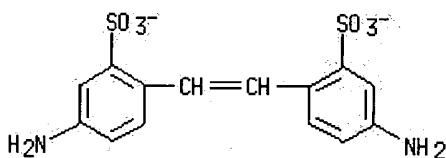
CMF C14 H32 N2



CM 2

CRN 50567-28-7

CMF C14 H12 N2 O6 S2



2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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=> fil reg; d acc 105337-96-0; fil CAOLD

FILE 'REGISTRY' ENTERED AT 03:55:51 ON 26 APR 2004

ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 105337-96-0 REGISTRY

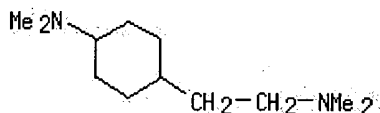
CN Cyclohexaneethylamine, 4-dimethylamino-N,N-dimethyl-, dihydrochloride (6CI) (CA INDEX NAME)

MF C12 H26 N2 . 2 Cl H

SR CAOLD

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS

(\*File contains numerically searchable property data)



# 2 HCl

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

FILE 'CAOLD' ENTERED AT 03:55:52 ON 26 APR 2004

=> fil reg; d acc 109220-13-5; fil CAOLD

FILE 'REGISTRY' ENTERED AT 03:56:00 ON 26 APR 2004

ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

RN 109220-13-5 REGISTRY

CN (1,4-Cyclohexyleneethylen)bis[trimethylammonium chloride] (6CI) (CA INDEX NAME)

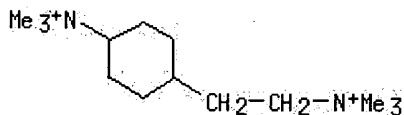
MF C14 H32 N2 . 2 Cl

SR CAOLD

LC STN Files: BEILSTEIN\*, CAOLD

(\*File contains numerically searchable property data)

CRN (122802-56-6)



# 2 Cl-

2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

FILE 'CAOLD' ENTERED AT 03:56:00 ON 26 APR 2004

=> fil reg; d acc 122802-57-7; fil CAOLD

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ANSWER 1 REGISTRY COPYRIGHT 2004 ACS on STN

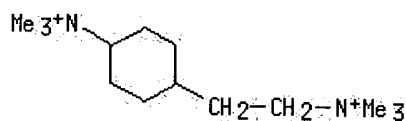
RN 122802-57-7 REGISTRY

CN (1,4-Cyclohexyleneethylen)bis[trimethylammonium] 4,4'-diamino-2,2'-stilbenedisulfonate (6CI) (CA INDEX NAME)

MF C14 H32 N2 . C14 H12 N2 O6 S2  
 SR CAOLD  
 LC STN Files: BEILSTEIN\*, CAOLD  
 (\*File contains numerically searchable property data)

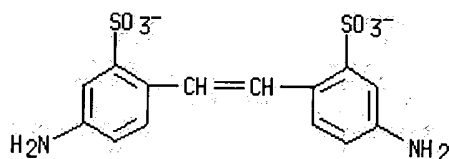
CM 1

CRN 122802-56-6  
 CMF C14 H32 N2



CM 2

CRN 50567-28-7  
 CMF C14 H12 N2 O6 S2



2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
0.42	468.23

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-40.19

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STN INTERNATIONAL LOGOFF AT 03:56:32 ON 26 APR 2004